

The use of bridged bicyclic molecules as models for the study of chemical reactivity

(L'UTILISATION DES MOLECULES BICYCLIQUES
PONTEES COMME MODELES
POUR L'ETUDE DE LA REACTIVITE CHIMIQUE)

THESE

présentée à la Faculté des sciences de l'Université de Genève
pour obtenir le grade de docteur ès sciences chimiques

par

François Denis DELAY

de

PROVENCE (Vaud)

Thèse N° 1638

GENEVE
Editions Médecine et Hygiène

1974

UNIVERSITE DE GENEVE
Département de chimie organique

FACULTE DES SCIENCES
Professeur C.W. JEFFORD

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La Faculté des sciences, sur le préavis du professeur C.W. Jefford, directeur de thèse, et d'une commission composée du professeur K. Schaffner (Faculté des sciences) et de Monsieur V. Rautenstrauch (docteur ès sciences chimiques/Firmenich S.A.), autorise l'impression de la présente thèse, sans exprimer d'opinion sur les propositions qui y sont énoncées.

Genève, le 25 janvier 1974

Le doyen :
Jean Muller

Thèse No 1638



This work has been carried out in the laboratories of the Department of Organic University of Geneva, under the direction of Professor C.W. Jefford during the period 1969-1973.

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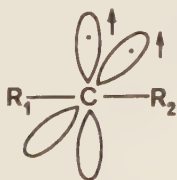
RESULTS AND DISCUSSION

1. Dihalocarbene: a useful chemical "building block"

1.1. Theoretical aspects

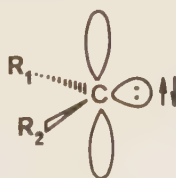
1.1.1. Nature of divalent carbon [43]

Carbenes are known to be reactive electron deficient intermediates. According to hybridization theory, one may expect two accessible but chemically different ground states for carbenes, singlet and triplet. Triplet divalent carbon should exhibit linear geometry with two equivalent and mutually perpendicular p orbitals, each containing one of the two unpaired electrons. The molecule has thus pronounced diradical character (figure 1a). The singlet species, however, can be regarded as an essentially sp^2 hybridized carbon with one of its σ orbitals filled with two paired electrons and with a vacant p orbital. This species corresponds to a model in which a carbonium ion and a carbanion are superimposed (figure 1b) [44].



- . $R_1 - C - R_2 = 180^\circ$
- . group of symmetry: $D_{\infty h}$
- . triplet
- . diradical

1a



- . $R_1 - C - R_2 = 120^\circ$
- . group of symmetry: C_{2v}
- . singlet
- . carbocation-carbanion

1b

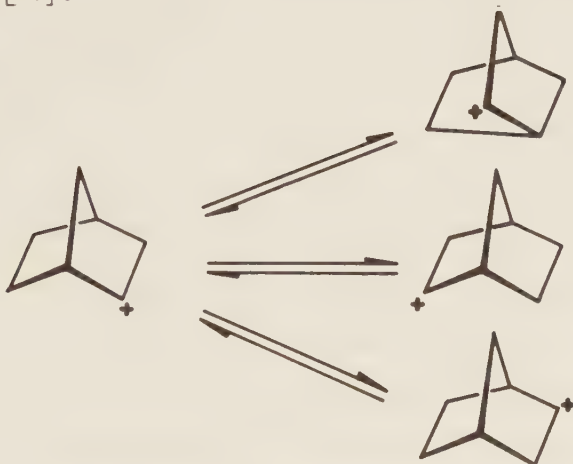
Figure



From the late forties to date, the study of chemical reactivity has been guided, in most cases, by the availability of suitable substrates and the degree of sophistication of analytical techniques. Thus, although the geometry of the steroids was quite suitable for the study of neighbouring double bond participation [12]-[14] or homoallylic reactivity [15] in solvolytic reactions, the advent of more advanced physical methods for separation (gas chromatography) and structure elucidation (IR, UV, MS and NMR spectroscopies) of products led chemists to work with smaller and more versatile molecules.

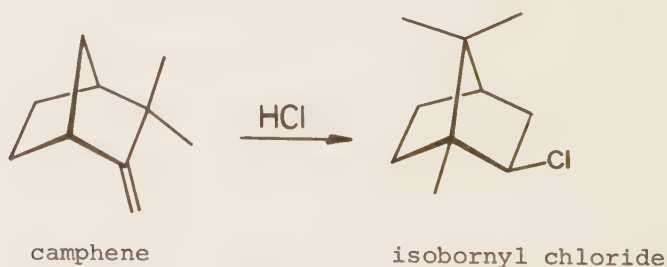
As bridged bicyclic monoterpenes of the camphene and pinene type undergo numerous complex skeletal modifications, the readily available and structurally related molecule norbornene [16] proved to be the substrate of choice. Protonation of this molecule gives the 2-norbornyl cation, which was formulated as early as 1949 as a non-classical species containing a plane of symmetry [17]. Furthermore, it was later demonstrated that this cation rapidly undergoes Wagner-Meerwein rearrangement, 6,2- and 3,2-hydride shifts at room temperature [18] [19]. A characteristic feature of this carbonium ion is that the structures resulting from these rearrangements all possess the

same skeletal type, in other words, the 2-norbornyl cation is degenerate [20].



It is also true that norbornene and its higher homologue bicyclo[3.2.1]octene have received much attention as models of reactivity, on account of the rigid conformation of their cyclopentyl and cyclohexyl moieties [21]-[24]. Furthermore, norbornene and its derivatives display the peculiarity of exo-stereoselectivity in addition and substitution reactions [25]-[31], which has been variously interpreted in terms of steric hindrance [32]-[34], torsional interactions [35] [36], polar effects [37] and stereoelectronic factors [38]-[40]. Our interest in the synthesis and chemistry of bicyclo[3.2.1]octane and bicyclo[4.2.1]nonane derivatives is connected with the as yet unresolved problem of exo/endo steric impediment in norbornene and related structures [41] [42]. Moreover, such common ring systems constrained by bridging constitute excellent models for the study of reactivity-structure relationships.

At the same time the first discoveries of molecular rearrangements were made, especially the remarkable 1,2-shift observed by Wagner and Meerwein in the bridged bicyclic monoterpenes [3].



With the enormous expansion of steroid chemistry, skeletal rearrangements in the terpene series received considerable attention [3]-[10] and the modern concept of classical and non-classical carbonium ions were introduced; the first formulation of the non-classical species was postulated by Nevell [11]

The determination of the ground state of substituted carbenes has received much attention in the last few years. Spectroscopic analyses of the simplest carbene, methylene, showed clearly that this intermediate exists in a nearly linear triplet configuration, which in all probability can be considered as the ground state [45]. More recent calculations were made by Hoffmann [46] and proved to be in good agreement with the spectroscopic results.

The substitution of one or both hydrogens in methylene by other groups modifies the nature of the ground state. Thus, both calculations [46][47] and spectroscopic data [48][49] have shown that CF_2 and most likely CCl_2 , CBr_2 and CHF are ground-state singlets. Bond angles of dichloro and dibromocarbenes in their lowest singlet state have been calculated and have been found to be 112° and 114° respectively.

The charge distribution in the series CH_2 , CHF and CF_2 has been described in detail by Harrison [50]. His analysis indicates an increased delocalization of the σ electrons in the halocarbenes compared to that in CH_2 , and a simultaneous influx of π electrons from the fluorines into the empty p orbital of the carbon. Thus, as the electrophilic character of carbenes is usually associated with this p orbital [51], it results that the electrophilicity should decrease along the series $\text{CH}_2 > \text{CHF} > \text{CF}_2$. In addition, we would also expect an increase in electrophilicity in going from CF_2 to CCl_2 and CBr_2 .

1.1.2. Generation of dihalocarbenes

As a large number of methods for the generation of each type of carbene are mentioned in the literature [43], this section is limited to the generation of dichloro and dibromocarbenes which were used in this work.

The classical way to generate dihalocarbenes consists of the interaction of a strong base with a haloform [52] or a tetrahalomethane [53].



In the case of dichlorocarbene, an improved method was found by Parham and Schweizer [54], who generated CCl_2 by decomposing ethyl trichloroacetate with sodium methoxide:



This method was then optimized for the addition of CCl_2 to norbornene [55]. The disadvantage of these methods lies in the fact that they are unsatisfactory for base-sensitive substrates. Consequently, it was necessary to develop a preparation involving neutral conditions. The thermal decomposition of sodium trichloroacetate [56] was found to be of little value, except in the presence of reactive and unhindered olefins [57].



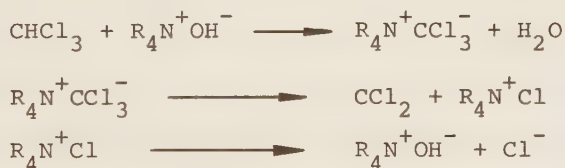
A more convenient method was provided by the thermolysis of organometallic reagents, such as organosilicon derivatives [58]



and particularly organomercuric compounds [59]. The decomposition of either phenyl(trichloromethyl) or phenyl(tribromomethyl) mercury in refluxing benzene gave excellent yields of dihalocarbene adducts with most olefins:



A recent method involving aqueous conditions has been reported and appears to be very promising [60] [61]. The interaction of chloroform with 50% aqueous sodium hydroxide in the presence of a quaternary ammonium salt as a phase transfer agent led to particularly high yields of the dichlorocarbene adducts (72% with cyclohexene; 80% with styrene). The following mechanism was suggested :



The quaternary ammonium salt is responsible for the transfer of the trichloromethyl anion from the aqueous surface into the organic phase.

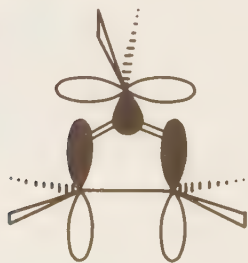
The wide choice of preparative methods makes dihalocarbenes one of the most useful reagents for ring enlargements. This fact will be amply demonstrated and described in the following sections.

1.1.3. Formation of three-membered rings

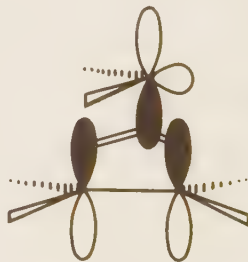
In order to understand the problem of dihalocarbene addition to any double bond, it is necessary to know if the reactive species is free or complexed. The study of relative reactivities of CCl_2 , generated by pyrolysis of CHCl_3 at high temperatures, towards olefinic substrates, provided a clear answer to this question [62]. These results showed that the free carbene was the reactive species in most cases. Seyferth [63] came to a similar conclusion by studying the kinetics of the thermal decomposition of organomercury derivatives.

The addition of dibromocarbene to cis- or trans-2-butene takes place stereospecifically to give the cis- or trans-1,1-dibromo-2,3-dimethylcyclopropane respectively [51]. This observation precluded the intermediacy of a triplet carbene leading to a diradical intermediate [64].

These experimental facts led chemists to interpret the addition of a singlet carbene to an olefin in terms of a concerted $[2 + 2]$ cycloaddition, or more precisely as the inverse of a cheletropic fragmentation [65]. Such a process can be visualized here in either of the two following modes.



2a, linear cheletropic addition



2b, non-linear cheletropic addition

Figure

The linear cheletropic addition (figure 2a) was found to be symmetry forbidden and, consequently, the non-linear cheletropic addition (figure 2b) appeared to be favoured [66]. The transition state exhibits a Hückel topology, in which the two paired electrons of the carbene are not involved. In this process, the carbene lies parallel to the plane of the double bond and is probably unsymmetrically disposed with respect of steric interactions of the carbene substituents [67].

According to Hoffmann [66], singlet carbene adds stereospecifically, not because it is a singlet, but because it can correlate with the ground state of a cyclopropane. It was recently proposed [68] that the allowed non-linear approach describes best the initial geometry but that the forbidden, more product-like, linear geometry is adopted in a later stage of the addition.

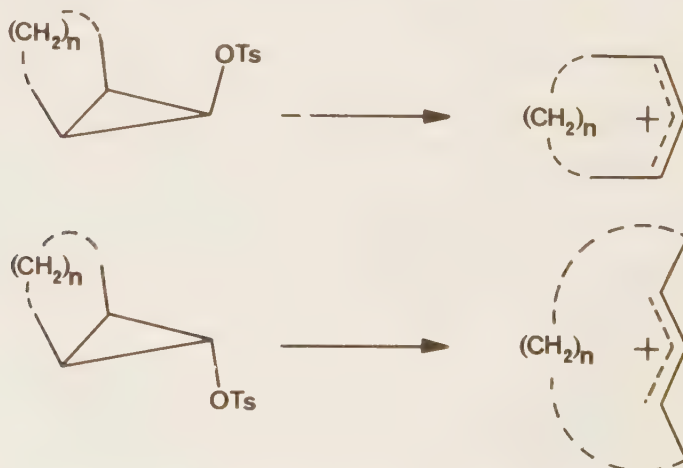
It is difficult at this stage to give a definitive interpretation of these carbene additions. Uncertainty still persists. For example, Anastassiou [69] reported that "symmetrical addition of a more energetic linear singlet methylene to ethylene is both allowed by symmetry and in some cases, plausible energetically."

1.2. Dihalocarbene addition to bridged bicyclic molecules

1.2.1. Addition of carbenes to norbornene

Addition of dihalocarbenes to acyclic olefins often yields surprisingly stable adducts [70]. In the cyclic series, however, the size of the ring has a substantial effect on the stability of these dihalocyclopropane derivatives.

Solvolytic studies have shown that the conversion of a cyclopropyl to an allyl cation is a concerted process [71]. Two disrotatory modes are possible. When substituents are cis to the leaving group, their rotation inwards is permitted and yields a cis,cis-allyl cation. When substituents are trans to the leaving group, they can rotate outwards and give the more stable trans,trans-allyl cation. Trans derivatives solvolyse much faster than the cis homologues.

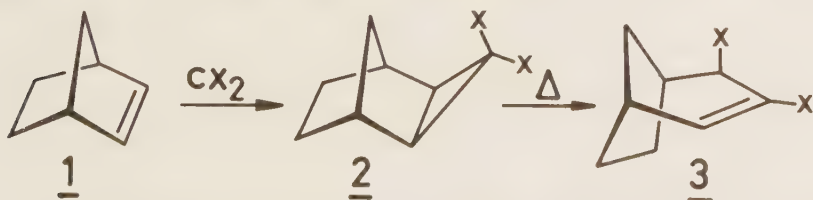


Incorporation of the cyclopropyl tosylate into a bicyclo-[n.1.0] alkyl system reverses the order of reactivity. If the ring is small, a trans,trans-allyl cation cannot be accomo-

dated, but a *cis,cis*-cation can.

Thermal cyclopropyl-allyl rearrangement of dihalocarbene adducts to cyclic olefins was similarly interpreted in terms of a concerted opening of the cyclopropyl cation [72]-[76]. The effect of ring size on the product distribution was clearly demonstrated. Thus, the thermal rearrangements of the dihalocarbene adducts to four-, five-, six- and seven-membered rings give exclusively *cis,cis*-allylic compounds. The next two higher homologues exhibit a more complex behaviour and yield mixtures, which are difficult to rationalize. However, a large system such as 2,2-dibromobicyclo[7.1.0]decane rearranges at 185° and gives only one product, *trans*-2,3-dibromodec-1-ene. On further heating at 185°, this kinetic product is converted into the thermodynamically more stable *cis* isomer.

Bicyclo[2.2.1]heptene, a constrained molecule, is of great interest as a substrate for carbene additions by virtue of both its chemical reactivity and synthetic value. Several independent research groups reported almost simultaneously their results on dihalocarbene addition to norbornene [77]-[79]



In agreement with the well-known peculiarity of norbornene to display an exo stereoselectivity towards electrophiles, dihalocarbenes similarly add exclusively on the exo face of

the molecule. The resulting tricyclic compound 2 is isolable under mild conditions [67] [80]. Heating 2 results in its stereospecific isomerization to the thermodynamically more stable exo allylic compound 3. This rearrangement occurs at room temperature for both the dibromo and dichloro derivatives. The driving force for this cyclopropane ring opening can be attributed to the steric interaction between the syn-halogen and the methylene bridge. Furthermore, the eclipsed boat-like geometry in 2 is energetically unfavourable.

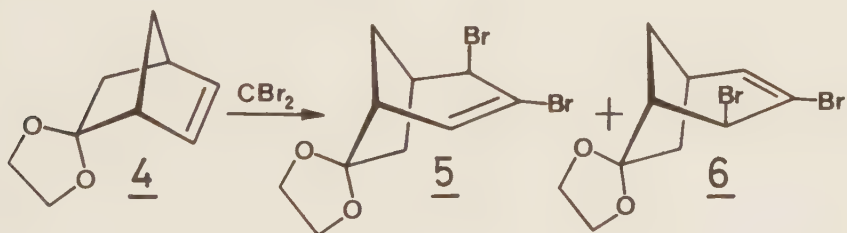
Apart from these conformational considerations, very little information about the intrinsic nature of this transposition was available. It appeared therefore of fundamental interest to further investigate the geometry constraints and electronic effects, which obviously play an important role in the addition and rearrangement processes.

1.2.2. Steric and electronic effects of substituents

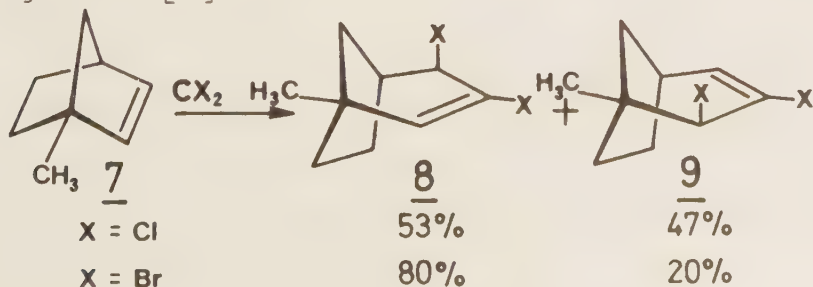
In the thermal opening of the cyclopropane adduct 2, either of the halogen leaving groups X could undergo the migration to the allylic position. Consequently if an unsymmetrical carbene such as CXY is used, then the mode of opening of the three-membered ring can be easily followed. Furthermore, it is possible to obtain information on the mode of addition of the carbene to the olefin in the first place. The results obtained from these unsymmetrical adducts show that the cyclopropyl-allyl transposition occurs in such a way that the group

which migrates is the one which is disposed syn. In other words, the principle of least motion has been obeyed. Another point is that the adduct itself 2 possesses C_s symmetry, but the products of rearrangement are enant iomeric [81].

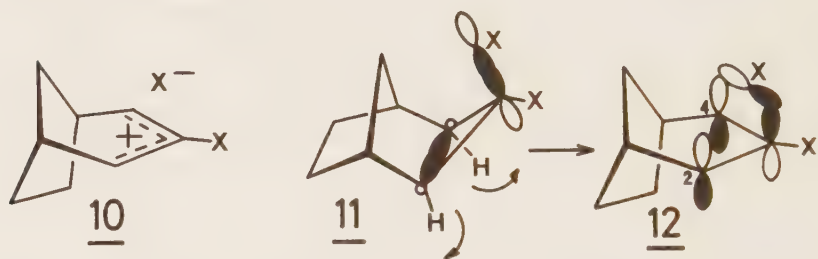
The suitable introduction of a substituent in the cyclohexene moiety of the norbornene skeleton changes the C_s symmetry and thus should provide a way of distinguishing the products of rearrangement. An ethyleneketal group situated at a reasonable distance from the double bond, as exemplified by compound 4, did not have any directive influence on the product distribution of the dibromocarbene addition. Both dibromo isomers 5 and 6 were found in a 1 : 1 ratio [82]:



The presence of a methyl group closer to the reactive site as in 1-methylnorbornene, resulted in a detectable steric effect. As expected, this effect increased with the size of the halogen atom [83]:



In summary, the findings enable two hypotheses to be advanced concerning the nature of the rearrangement. First of all, the formation of an intermediate ion pair such as 10 can be envisaged, in which the anion was originally the syn-halogen. Recombination of the two ions can then take place either on carbon C2 or on carbon C4, depending on their respective steric environment.



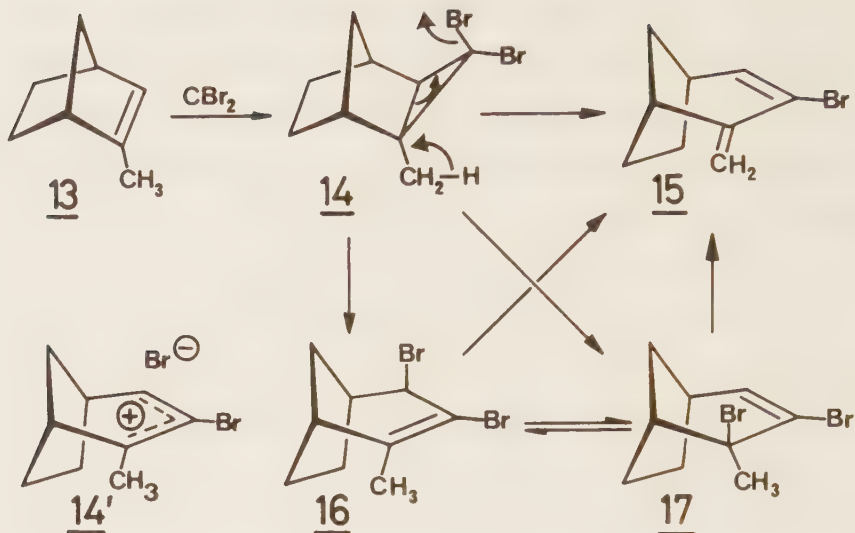
Secondly, a fully concerted non-ionic mechanism is also possible. The migrating halogen can participate with both lobes of its atomic orbital in a [1,3] suprafacial sigmatropic shift [68]. As four electrons are involved in this process (11→12), the transition state requires a basis set of atomic orbitals having Möbius topology [81]. This can be readily achieved by breaking the C2 - C4 bond in the disrotatory mode, which is allowed by the geometry of the molecule. It is worthwhile to point out here that the process is tantamount to a nucleophilic substitution by chlorine on one face of C4 with concomitant departure of the C2 - C4 sigma bond. At the same time, this sigma bond attacks in backside fashion the C3 carbon from which the halogen is in the process of leaving. In other words,

this is a typical diplotropic rearrangement. In this concerted process, steric factors will determine the choice of carbon C2 or C4. One must point out here, that the results obtained so far do not permit an unequivocal decision between these mechanisms.

As the methyl group at the bridgehead position in 7 exhibit apparently only a steric effect on the course of the cyclopropyl-allyl rearrangement, it was tempting to introduce a substituent directly on the double bond. This would cause mainly an electronic effect, which could possibly provide a useful insight into the mechanism.

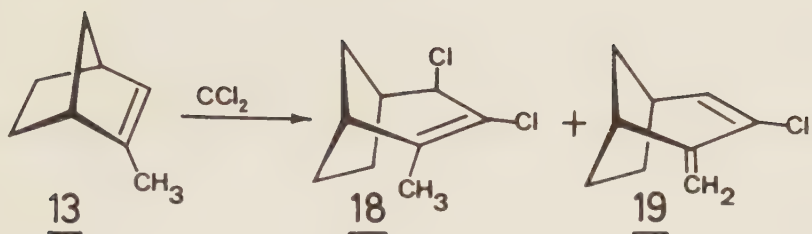
1.2.3. Dichlorocarbene addition to 2-methylnorbornene

The use of 2-methylnorbornene (13) in the study of dihalocarbene additions to olefins provided an opportunity to investigate the competition between the thermal cyclopropyl-allyl rearrangement and the elimination of hydrogen halide. The addition of dibromocarbene to 13 resulted in the isolation of a sole product, 3-bromo-2-methylenebicyclo[3.2.1]oct-3-ene (15) [83]. This result was interpreted by assuming that elimination always occurred prior to rearrangement of the cyclopropyl ring to the allylic product. Elimination could occur directly from 14 to give 15. Or 14 could undergo ring opening to the intermediate ion pair, 14' which could subsequently lose a proton. However, from the mechanistic point of view, alternatives have to be considered.



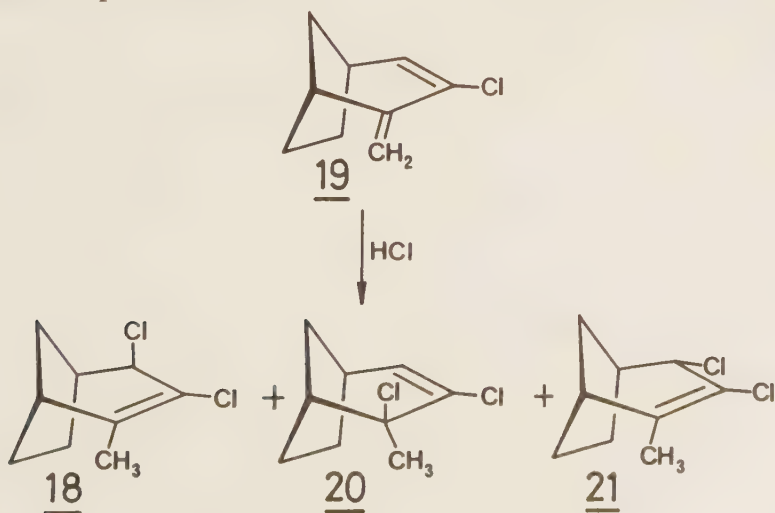
Firstly, the tricyclic compound **14** can undergo rearrangement and elimination in a concerted fashion. Secondly, rearrangement occurs prior to a 1,4- or a 1,2-elimination of HBr from compounds **16** or **17** respectively. Furthermore interconversion of one isomer into the other by a [1,3] suprafacial sigmatropic shift is also possible. In order to test the existence of these alternatives, we decided to make the chlorine analogues of **14**. [84]

Generation of dichlorocarbene in the heterogeneous aqueous chloroform medium [60] in the presence of **13** affords a mixture of *exo*-3,4-dichloro-2-methylbicyclo[3.2.1]oct-2-ene (**18**) and the expected diene **19** in 51% and 10% yield, respectively. The dichloro compound exhibits remarkable stability. When heated at 140° in 1,2,3-trimethylbenzene, it undergoes a partial 1,4-elimination of hydrogen chloride to give **19**.



The elimination in pyridine is most facile and proceeds to completion at 110° . These stability tests argue strongly against the formation of the diene 19 from the dichloro compound 18 under the conditions used for the carbene addition. Consequently, we cannot rule out definitely the formation, in a concerted fashion, of the tertiary chloride 20. In order to check its existence and to investigate its chemical behaviour, we tried to prepare it by an alternative route.

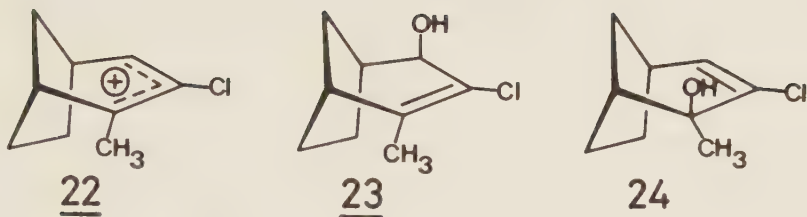
Addition of hydrogen chloride to the diene 19 in carbon tetrachloride at -10° results in a mixture of 1,2- and 1,4-addition products:



The reaction was monitored by NMR and showed, after complete disappearance of the starting diene, a mixture of 18, 20 and 21 in the ratio 3 : 1 : 1. On letting the solution reach room temperature compound 20 is completely converted into the more stable isomer 18. As the medium is saturated with HCl, none of the elimination product 19 was detected. Repetition of this experiment at 45° with chloroform as solvent shows the quantitative conversion of the diene 19 into 18 and 21 in the ratio 4:1.

These results support the hypothesis of the concerted formation of 20 as a kinetic product in the cyclopropyl-allyl rearrangement. Depending on the conditions, this tertiary chloride (20) can then undergo either a [1,3] suprafacial sigma-tropic shift to give 18, or a 1,2-elimination to yield the diene 19. This last mechanism was verified by Brun and Waegell who, concurrently succeeded in isolating 20 directly from the carbene addition mixture at a lower temperature than reported here [85].

The best way to account for the formation of the endo compound 21 is to assume the formation, in a first step, of the allylic cation 22 by protonation of the exocyclic methylene group in 19. The nucleophilic attack of the chloride ion then takes place on carbons C2 and C4. The endo attack is rather surprising in view of the exo stereoselectivity common to these systems.



Chemical evidence for the formation of cation 22 is provided by the hydrolysis of 18 in 65% aqueous acetone at room temperature. A mixture of both alcohols 23 and 24 in the ratio 3:1 is isolated in high yield. Under stronger conditions such as refluxing a solution of 18 and silver nitrate in 50% aqueous acetone, the tertiary alcohol 24 is not isolated but rather 34% of the diene 19 is formed.

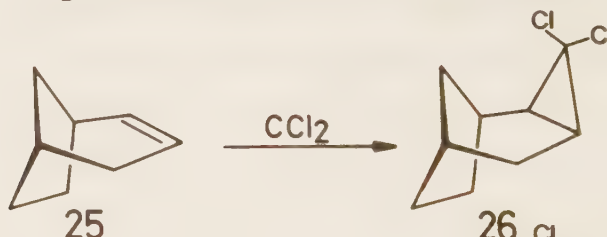
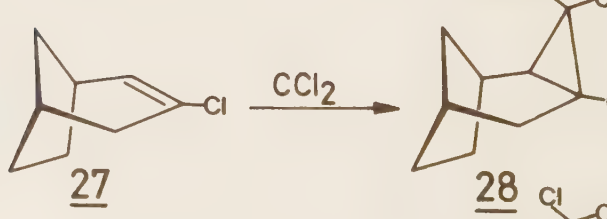
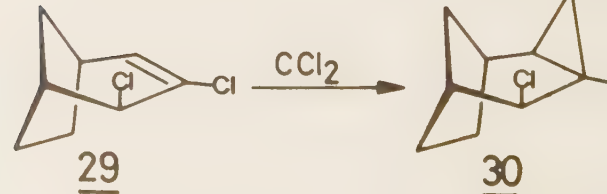
An interpretation for the formation of the endo compound 21 is that Cl^- can undergo equilibration to give both 18 and 21. Whereas OH^- is a poor leaving group and once it is fixed to the exo side it has no chance under neutral or alkaline conditions to migrate to the endo side on account of its inability to ionize.

1.3. Entries to bicyclo[4.2.1]nonane derivatives

1.3.1. Di-, tri- and tetrachlorotricyclo[4.2.1.0^{2,4}]-nonanes

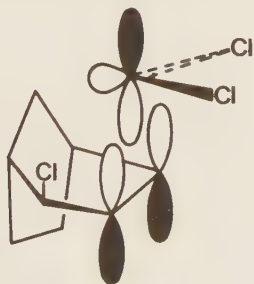
As has been seen in the preceding sections, dichlorocarbene adds readily to norbornene derivatives to give tricyclic adducts, which can undergo thermal rearrangement. Thus, the optimization of this method should make bicyclo[3.2.1]octene derivatives readily accessible. In order to explore the applicability of this route to the synthesis of the next higher homologues, bicyclo[4.2.1]nonenes, we decided to study the addition of dichlorocarbene to bicyclo[3.2.1]oct-2-ene (25), and its monochloro (27) and dichloro (29) derivatives.

Table 1: CCl₂ additions to bicyclo[3.2.1]octenes

		<u>YIELD (%)</u>
		94
		89
		46

The interaction of an excess dichlorocarbene, generated by decomposition of ethyl trichloroacetate in presence of sodium methoxide [55] with 25, 27 and 29, gave the respective adducts 26, 28 and 30 (Table 1). No product of rearrangement is isolated. The exo conformation is assigned to all three cyclopropane derivatives by analogy with the norbornene case. This supposition is well supported by the fact that dichlorocarbene adds to 25 and 27 more readily than to 29. The exo-3,4-dichloro derivative 29 presents an obstacle on the exo face to the incoming dichlorocarbene. Assuming a non-linear cheletropic approach, it can be seen that the exo allylic chlorine will engender repulsive non-bonding interactions with the carbene in the transition state (figure 3).

Figure 3



Evidence for the exo configuration is based mainly on its NMR spectral properties. The observed shielding of the anti proton of the methylene bridge can only be due to the ring current of an exo disposed cyclopropane. Taking the chemical shifts of the corresponding proton in bicyclo[3.2.1]octene derivatives (1.37 ppm) as reference [86] [87], the upfield shifts observed in 26, 28 and 30 are 0.32, 0.30 and 0.22 ppm respectively.

From a synthetic point of view, it appeared worthwhile to see if a consecutive double addition of dichlorocarbene to norbornene would occur. The most appropriate method in this case would be to generate CCl_2 in the heterogeneous aqueous chloroform medium [60], as the relatively high temperature required (40°) should ensure the thermal rearrangement of the first adduct. The tetrachloro compound 30 is indeed isolated, but only in 10-12% yield after 24 hours. Concurrently with our work, Kraus obtained the product in a good yield (68%), when carrying out the reaction at room temperature for a much longer period of time (72 hours) [88].

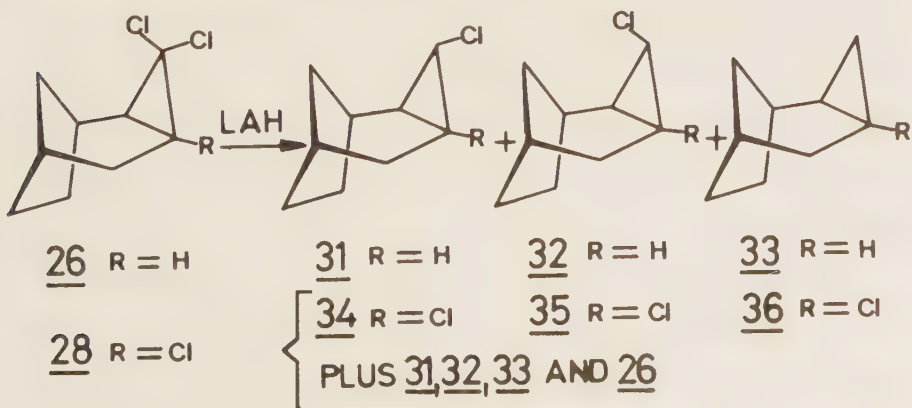
1.3.2. Reactivity of cyclopropyl and bridgehead halides towards metal hydrides

Reductive dehalogenations of organic chlorides are usually carried out by means of the dissolving metal technique or by means of lithium aluminium hydride. However, lithium aluminium hydride is chiefly used for those organic halides which can undergo an $\text{S}_{\text{N}}1$ or $\text{S}_{\text{N}}2$ process [89] [90]. The method of choice for the reductive dehalogenation of so-called inert halides is that which uses organotin hydrides [91]. Organotin hydride reductions are thought to involve radical intermediates [92] and this explains perhaps why bridgehead halides, for example, which can form bridgehead radicals, undergo reduction. However, examples have been reported in which LAH was found to reduce gem-dihalocyclopropanes [93] [94] [95]. Moreover, it has

been shown in these laboratories that 1-bromoadamantane was readily reduced by LAH in high yield. This result can be explained by a nucleophilic displacement of the bromide in the contact ion pair, as the adamantyl cation appears to exemplify limitive carbenium ion stability [96].

However, it appears from these indications that LAH could well be applicable for the reduction of not only other bridgehead halides, but also for cyclopropyl halides in general. Accordingly, di-, tri- and tetrachloro tricyclic compounds 26, 28 and 30 should be good models for the study of the relative reactivities of cyclopropyl, bridgehead and alkyl chlorides towards lithium aluminium hydride.

Treatment of 26 with excess LAH in refluxing tetrahydrofuran for 27 hours gave a mixture of the two monochloro isomers 31 and 32 together with the parent hydrocarbon 33 in the percentage ratio 58.5:29.2:12.2.



The presence of a third chlorine at the bridgehead position of the cyclopropane in 28 increases substantially the

reactivity of the geminal cyclopropyl halogens. Thus, the reduction process takes place already in boiling ether. After 45 hours, the disappearance of the starting material was complete. Analysis of the resulting mixture by gas chromatography reveals seven products. Separation and identification gives 34, 35 and 36 in the ratio 45.8:22.9:7.0 respectively and also 24.3% of the further reduced compounds 31, 32, 33 and 26. In this case, the syn/anti ratio obtained for the reduction of the cyclopropyl chlorines is identical with that found in the reduction of 26 (2:1). Furthermore, the bridgehead halogen proves to be far less reducible than the cyclopropyl halogens.

These results show unambiguously that LAH readily dechlorinates cyclopropyl chlorides without any opening of the three-membered ring. The question arises now, what is the mechanism for the reduction.

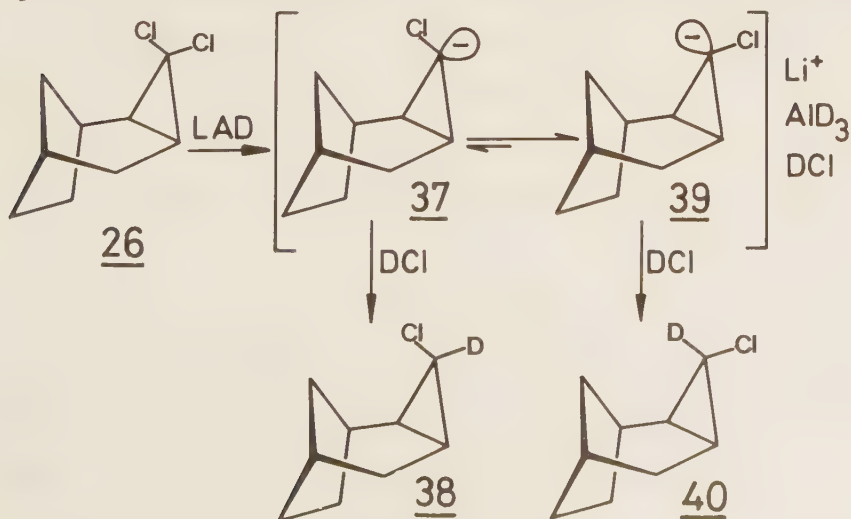
As an S_N1 mechanism would necessitate the intermediacy of a cyclopropyl cation, which would open instantaneously to an allyl cation [81] [97], this mechanism can be discarded. Moreover, both an S_N2 process and a four-center mechanism [98] are geometrically disfavoured [99], but have to be considered as possibilities.

Recently, it has been demonstrated in a parallel study that the reduction of gem-fluorochloro derivatives is a stereoselective process [100]. Thus, syn and anti isomers of bicyclic and tricyclic fluorochlorocyclopropanes were treated separately with LAH in diglyme at 100°. In each case, reductive

dechlorination occurred quantitatively to give a pair of fluoro epimers in which the original skeleton remains intact. The overall reaction course is one of retention of configuration at the fluorine-bearing carbon atom, except when the fluorine substituent encounters non-bonding interactions.

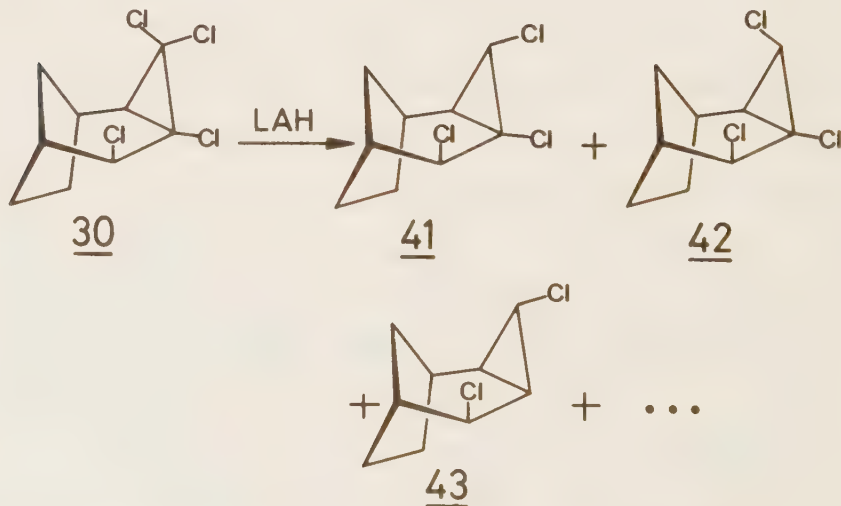
Two intermediates can account for this stereoselectivity; a cyclopropyl radical or carbanion. Both species tend to retain their configuration, but may invert under the pressure of non-bonded interactions.

Repetition of this experiment using lithium aluminium deuteride (LAD) allowed a radical mechanism to be discounted, as there was no incorporation of hydrogen from the solvent (diglyme). This strong indication of a carbanion mechanism led us to investigate the LAD reduction of 26. On treatment with excess LAD in boiling ether, the reduction products 38, 40 and the deuterated analogue to 33 were obtained in percentage ratios of 18, 74 and 8%.



Separation of both monochloro isomers 38 and 40, and inspection of their NMR spectra showed $92.0 \pm 5.0\%$ and $93.0 \pm 5.0\%$, respectively of deuterium incorporation. Obviously these results clearly support the carbanion mechanism already proposed.

Lithium aluminium hydride also proves successful for reductive dehalogenation of the tetrachloro tricyclic compound 30. This time, the overall reduction proved to be more sluggish than in the earlier cases and recourse to a higher boiling solvent had to be made in order to effect reduction. A complex mixture of thirteen reduced products was obtained. However, the major reaction course was monodechlorination. Compounds 41, 42 and 43 were found in yields of 44, 7.8 and 25% respectively.



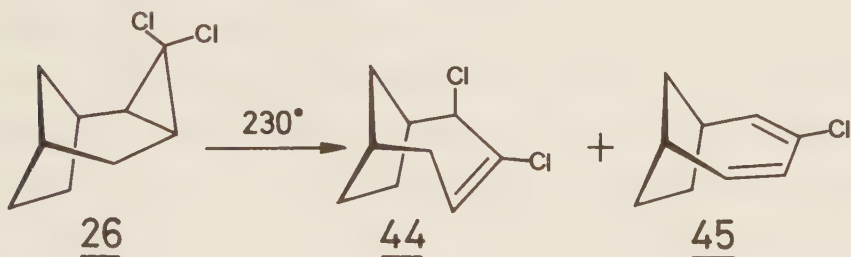
This result confirms our previous observations, namely the preponderant formation of the anti-chloro derivatives. Finally, this set of experiments allows us to establish the following

order of reactivity for the different chlorides in this series:

Cyclopropyl > bridgehead > alkyl

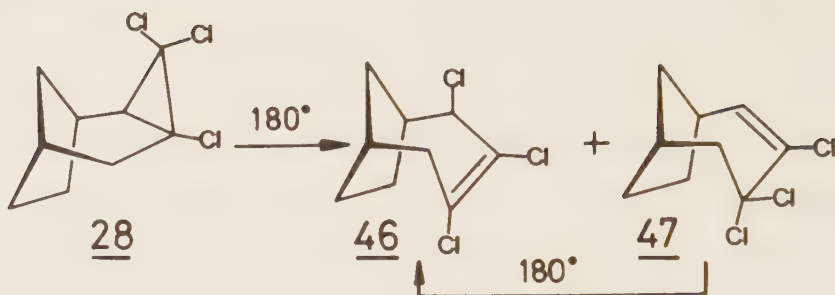
1.3.3. Thermal cyclopropyl-allyl rearrangements

One of the main features of interest in tricyclic compounds such as 26, 28 and 30 concerns, of course, their propensity to thermal rearrangement into the more reactive bicyclo[4.2.1]nonenyl chlorides. In all cases, high temperatures were required to bring about rearrangement of the three-membered ring in these compounds.



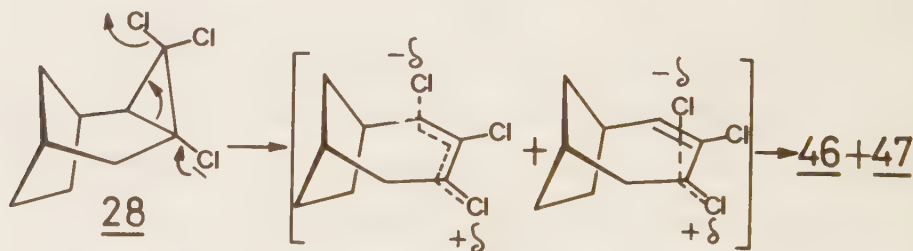
The cyclopropane ring in 26 opens at about 230° and gives 44 in 47% yield after two hours. Some of the diene 45 is also obtained together with some polymeric material. The fact that only one rearranged isomer (44) is isolated is attributed to the thermodynamic stability of the double bond between carbons C3 and C4. Further evidence for the stability of the double bond in this position is provided by the thermal rearrangement of the trichloro derivative 28. When treated at 180° in decalin for 18 hours, 3,3,4-trichlorobicyclo[4.2.1.0^{2,4}]nonane (28) gives a 2:1 isomeric mixture of 46 and 47 in 76%

yield.



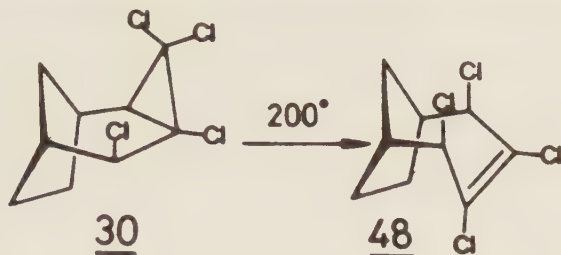
Further heating of this mixture at 180° results in the isomerization of 47 to 46.

In contrast with the dichloro derivative, 28 undergoes ring enlargement without substantial elimination of hydrogen chloride. The greater propensity of 28 to rearrangement compared to that for 26 can be rationalized possibly by invoking a mesomeric effect of the bridgehead halogen :



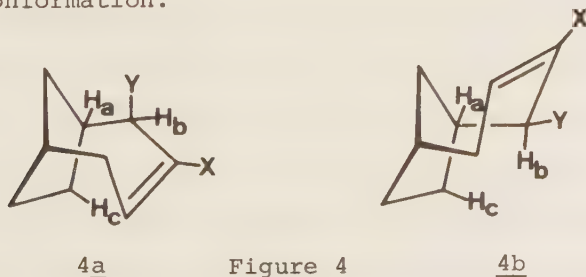
The tetrachloro derivative 30 had to be heated at 200° without solvent for 24 hours for ring opening to occur. Only one product was characterized, namely 48, which was obtained in 47% yield. In this case, the favourable electronic effect of the bridgehead chlorine is probably nullified by repulsive interactions in the transition state between the exo substi-

tuent on C4 and the migrating cyclopropyl chlorine.



It is interesting to note here that the order of increasing reactivities in these thermal rearrangements strictly parallels that observed in the reductive dehalogenations with lithium aluminium hydride, namely $\text{26} < \text{30} < \text{28}$.

Finally, we have to consider the conformation of these bicyclo[4.2.1]non-3-ene skeletons. While bicyclo[3.2.1]octene systems possess six- and seven-membered rings fixed in half-chair conformations, the larger bicyclo[4.2.1]nonene derivatives ought to exhibit greater flexibility. For derivatives 44, 46 and 48 two limiting conformations are conceivable (see figure 4). The cycloheptane moiety can adopt either a chair or a boat conformation.



If we consider the conformations preferred by the corresponding free monocyclic olefins, namely the chair form for

cycloheptene derivatives [101] and either the boat or chair form for cyclooctene [102] derivatives, we would expect conformation 4a to be favoured in the bicyclic cases. Unfortunately, the coupling constants $H_a H_b$ observed in all three compounds lie in the region 4.6-4.8 Hz. These values are consistent with the dihedral angles found in both limiting conformations 4a ($40-45^\circ$) and 4b ($115-120^\circ$) [103]. It was also found that the chemical shifts and coupling constants were insensitive to a temperature range of $0-100^\circ$, which also indicates that one conformation is favoured and that there is no tendency for any conformational equilibrium.

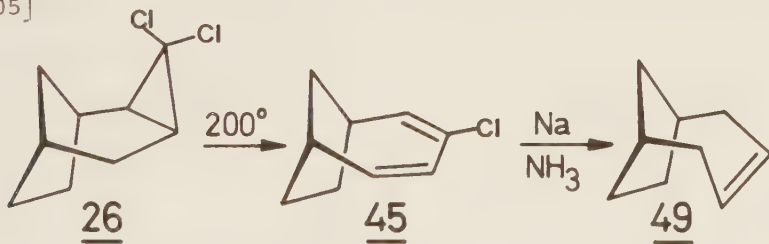
Finally, conformation 4a was assigned to 44, 46 and 48 on the basis of steric considerations. Inspection of a model of conformation 4b reveals unfavourable interactions between the allylic substituent Y and the vinylic substituent X. Furthermore, the pseudo-axial proton H_b encounters a steric repulsion with the endo ethylene proton H_c .

1.3.4. Bicyclo[4.2.1]nona-2,4-diene derivatives

We have shown in a previous section that under appropriate conditions, the various cyclopropane adducts with bicyclo[3.2.1]octene and its derivatives can be induced to rearrange with or without elimination. We now describe in this section how the products of rearrangement can be chemically converted to bicyclo[4.2.1]nona-2,4-diene and its derivatives. As will be mentioned later, these dienes are of photochemical interest.

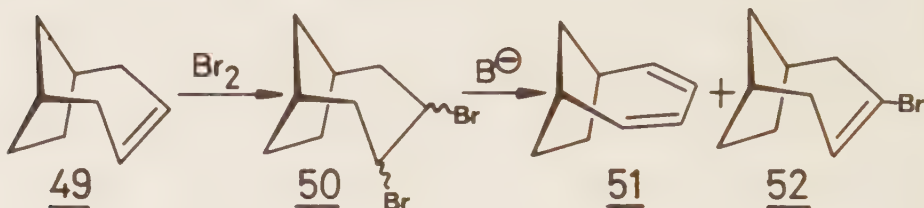
Very few syntheses in this series have been reported in the literature. A preparation of the parent diene (51) has already been reported by Frey [104], who carried out the diimide reduction on bicyclo[4.2.1]nona-2,4,7-triene.

It was previously observed that the thermal rearrangement of the cyclopropane adduct 26 was accompanied with a small amount of the monochloro diene 45. This elimination could be made the main course and if the vinylic chlorine could be removed, then here would be a good synthetic route to the parent diene 51. Treatment of 26 at 200° in quinoline for four hours gives 3-chlorobicyclo[4.2.1]nona-2,4-diene (45) in 79% yield [105]



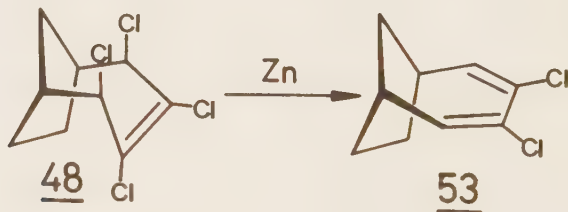
However, treatment of 45 with sodium in liquid ammonia gave only the mono-olefin 49 [106]-[108]. Not only did reductive dechlorination take place, but also the second double bond was reduced as well [109]-[112]. Nevertheless, the unexpected formation of 49 can be turned to advantage. The preparation of bicyclo[4.2.1]nona-2,4-diene (51) requires therefore two additional steps. Bromination of 49 gives presumably the trans-dibromo adduct 50 almost quantitatively. On treatment with potassium *t*-butoxide in dimethylformamide [113], the dibromide 50 undergoes elimination of hydrogen bromide and

affords a mixture of the expected diene 51 and the monodehydrobrominated compound 52 in 60% and 30% yields respectively.



Recently, the [7,8]-benzo derivative of 51 has been prepared by a similar route [114]. Treatment of the olefin corresponding to 49 with N-bromosuccinimide gave the allylic bromide, which on treatment with base gave the diene in 60% yield.

3,4-dichlorobicyclo[4.2.1]nona-2,4-diene (53) proved to be very readily accessible. Zinc initiated dechlorination of the tetrachloro compound 48 in acetone yields 53 quantitatively [115].



The ease with which this reaction proceeds is probably due to the excellent spatial disposition of both allylic chlorines for a concerted synfacial elimination.

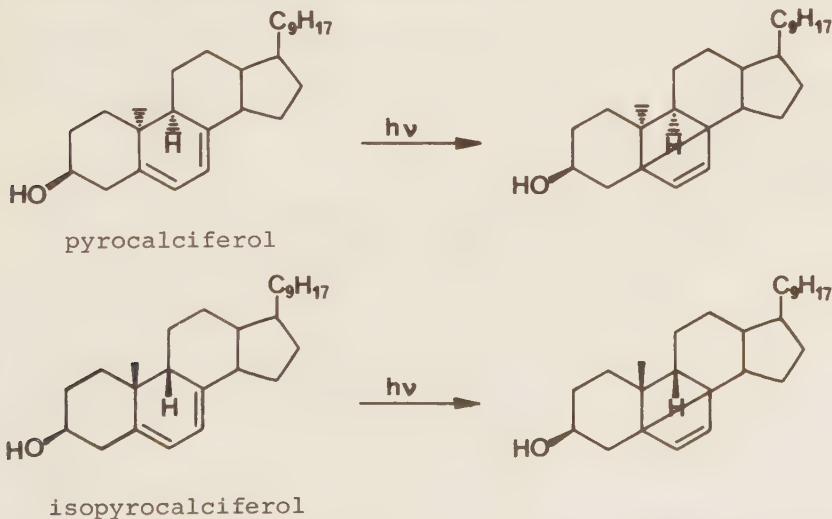
2. Electrocyclic closure in bicyclo[4.2.1]nona-2,4-dienes

2.1. Photochemical behaviour of conjugated dienes

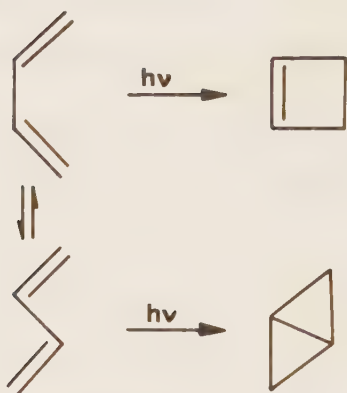
2.1.1. Internal [2+2] cycloadditions

Unsaturated systems can undergo photochemical [2+2] cycloadditions either intermolecularly (dimerization) or intramolecularly (valence isomerization) [116]. Irradiation of conjugated dienes in solution leads to cyclobutene derivatives, when the steric restrictions are not too severe [117] [118].

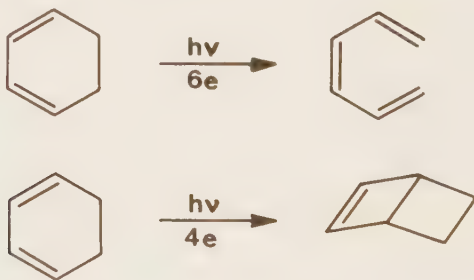
The first case of cyclobutene formation was discovered in the vitamin D series in the late fifties [119] and gave rise to increased interest in this field.



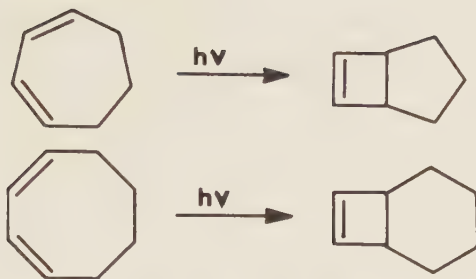
Irradiation of the simplest acyclic diene, butadiene, produces two valence isomers, cyclobutene and bicyclobutane. The products are thought to proceed from the cis and trans photoexcited states of the starting material [120] [121].



When conjugated dienes are incorporated in cyclic systems, the course of the photochemical reaction depends on the size of the ring. Thus, cyclohexa-1,3-diene on irradiation undergoes either ring opening through a transition state of six electrons [122], or ring closure through a transition state of four electrons [123] [124].



When the diene system is found in a medium ring such as cycloheptadiene or cyclooctadiene, ring scission cannot occur and only electrocyclic closure process is observed [120] [125] - [127].

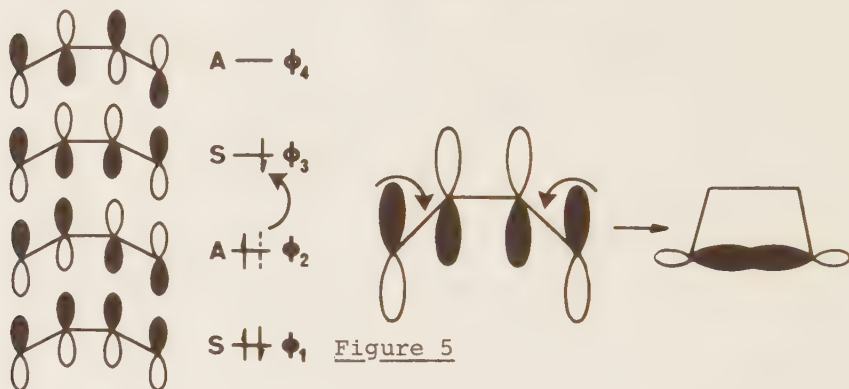


In both cases, ring closure occurs to give the cis product. Nevertheless, this would be the expected result in view of the geometric constraint in medium rings, which would not favour the formation of the trans isomers. Before we discuss the photochemical behaviour of bicyclo[4.2.1]nona-2,4-diene and its derivatives, which are of course constrained versions of cycloheptadiene or cyclooctadiene, it is well to consider the nature of the electrocyclic closure process in more detail.

2.1.2. The Woodward-Hoffmann rules and the nature of the excited states

The butadiene-cyclobutene interconversion has been the object of great theoretical interest [128]-[131]. According to Woodward and Hoffmann and later Longuet-Higgins and Abrahamson [132] [133], a concerted electrocyclization is governed by the conservation of the symmetry of the highest occupied molecular orbital along the reaction path. Photoexcitation of butadiene in the cisoid conformation promotes an electron from the ϕ_2 to the ϕ_3 molecular orbital, which is symmetric with respect to the median plane (see figure 5). Clearly, if symmetry is to

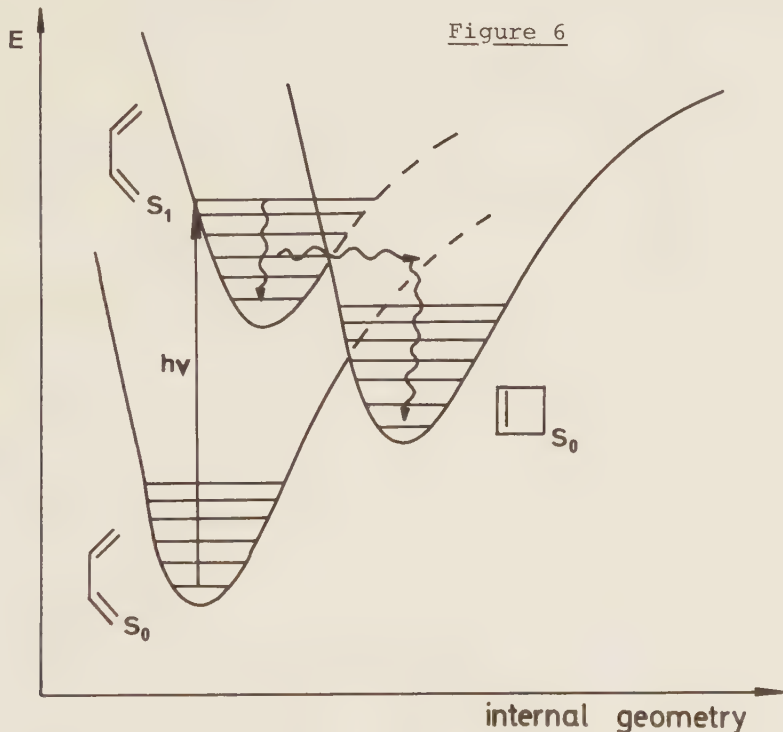
be conserved, then closure of the ends of the ϕ_3 molecular orbital will entail a disrotatory movement.



In spite of the great value of these predictive rules, the role of the nature of the excited state singlet or triplet has been ignored. The question remains as to whether the excited starting molecule gets to products in their excited or ground state.

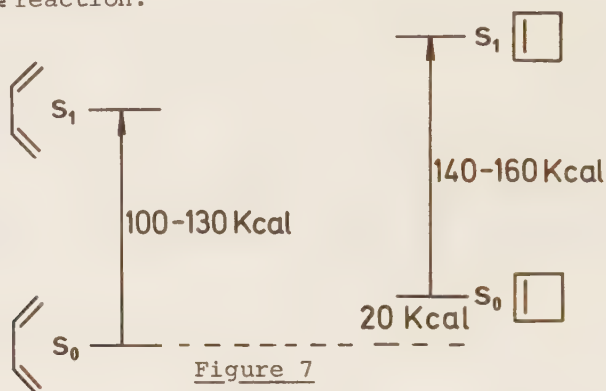
According to Dauben [134], the excitation process itself obeys the Franck-Condon principle. In other words, as the excitation process is faster (10^2 - 10^3 times) than the molecular vibration, almost no change in the relative position of the nuclei takes place during the period of absorption and excitation (see figure 6). Subsequently, the singlet alters its geometry to a non-Franck-Condon singlet by vibrational relaxation. As intersystem crossing ($S_1 \rightarrow T_1$) in dienes is known to be inefficient [120][135]-[140], reactions arising from a triplet state will be rare. Thus, it can be seen from figure 6 that the molecule in its excited singlet state can undergo

possibly an isoenergetic internal conversion and return to a ground state of either the starting material or the product [141].



These assumptions find support from a consideration of the energies of the various states involved. Knowing that the ground state cyclobutene is about 20 Kcal/mole less stable than butadiene, it follows that the excited singlet state of cyclobutene will be about 50-60 Kcal/mole higher in energy than the corresponding singlet of butadiene (100-130 Kcal/mole) (figure 7) [134]. Thus, the excited state of the diene has no chance to interact with an excited state of the same multiplicity in the product. Accordingly, the provenance of the

cyclobutene can only be the singlet state of butadiene and a crossover process as outlined by Dauben is the best way of explaining the reaction.



A different interpretation has been made recently by Oosterhoff [142]. He mapped out the potential energy surfaces which connect the ground and the first two excited states of butadiene and cyclobutene. For the cisoid conformation of butadiene, two excited singlet states exist which are symmetric and antisymmetric with reference to the mirror plane (figure8).

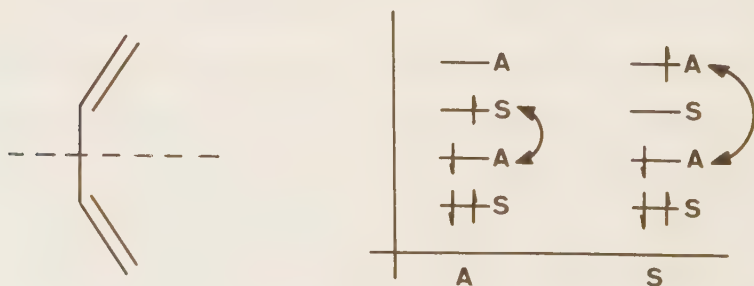
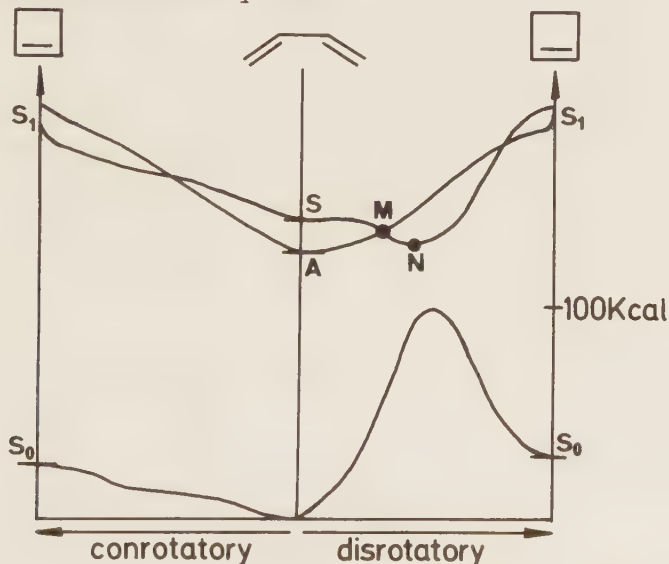


Figure 8

Moreover, he found that for all torsional variations from the cisoid geometry, the two excited states are always very close to each other in energy.

It is seen from figure 9 that a thermal disrotatory process would require a much higher activation energy (ca. 100 Kcal/mole) than a conrotatory process. On the other hand, photoexcitation of the diene will produce a singlet state in an energy level slightly above the energy hill of the thermally disallowed disrotatory mode.

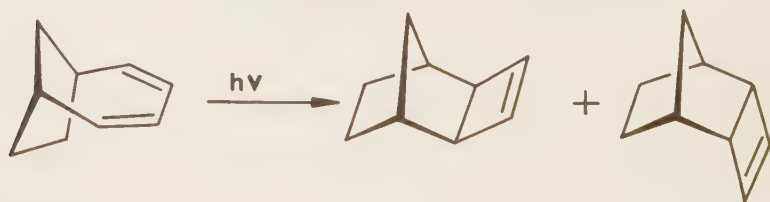
Figure 9



The essential point in this part of the diagram is that the antisymmetric and symmetric energy curves intersect (M). This allows a molecule in the antisymmetric state to pass adiabatically into the symmetric one, which can undergo disrotatory deformation. Excess vibrational energy will be dissipated by collisions and the molecule will reach the well (N) of the potential surface. As this molecule is in a conformation close to that of the disrotatory transition state, mixing with the ground state energy surface becomes thus feasible. The reaction can then either lead to cyclobutene or reform the diene.

This provides an attractive alternative interpretation of the Woodward-Hoffmann rules for concerted photoreactions. However, no account is taken of the multiplicity of the excited state. Basically, the difference between the singlet and triplet states is a change in the energy content of the molecule [145]. The energy level of the triplet is lower than that of the singlet. Consequently, the interaction between an excited triplet and the ground state of the disrotatory mode will even be greater. This may also explain why photosensitized irradiations of some conjugated dienes give cyclobutene derivatives in good yields and in higher purity than direct irradiations [137] [144].

We now come to the photochemical ring closure in bicyclo[4.2.1]nona-2,4-dienes which is expected to follow a disrotatory mode to give exo and endo cyclobutene derivatives.



In view of the known peculiarity of norbornene to display exo stereoselectivity, it should be interesting to see if the formation of the bicyclo[2.2.1]heptane skeleton has a directive effect on the formation of the products [145]. Calculations of strain energies show that the exo conformation

is preferred by ca. 5.0 Kcal/mole ^{1/2/}.

Lastly, the heavy atom chlorine is expected to play a role regarding the conversions of singlets to triplets.

2.1.3. The effect of a halogen substituent

McClure discovered that substitution of aromatic derivatives with elements of groups IV, V and in particular with halogens, so-called heavy atoms, caused a marked decrease in the triplet lifetime [146]. A similar effect was detected in the study of spin-relaxations in alkali vapors in a helium atmosphere [147]. These phenomena were interpreted in terms of spin-orbit coupling between the excited electron and the heavy atom. Such interactions enhance the usually forbidden $S \leftrightarrow T$ transitions. Experimental and theoretical aspects of intramolecular heavy atom effects have been abundantly reported [148]-[150]. The main results are based on the kinetics of radiative processes such as phosphorescence in aromatics [151] or thermoluminescence of inorganic salts [152].

When two colorless liquids, α -chloronaphthalene and ethyl iodide are mixed, a yellow color is formed, although no chemical reaction occurs. This experiment provided the first example of an intermolecular heavy atom effect, which was explai-

^{1/}I thank Dr. P. Gund from the Graphics Computer Laboratory, Princeton University, for these calculations.

^{2/}The program used was SYMIN (synthesis minimization).

ned as an ethyl iodide-induced $S \rightarrow T$ transition in α -chloronaphthalene [153].

Considerable effort has been expended in the investigation of similar heavy atom solvent effects [154]-[156]. Thus, the presence of a heavy atom in the proximity of the excited chromophore quenches the fluorescence emission and increases the phosphorescence yield, presumably due to an enhancement of intersystem crossing and the $T_1 \rightarrow S_0$ radiative process respectively [157].

As $S \leftrightarrow T$ transitions in n, π^* excited states are usually faster than those involving π, π^* excited states, no substantial heavy atom effect is detected in keto derivatives [158]-[160]

The relative importance of the heavy atom effect on radiative and radiationless processes remains however a matter of controversy. Thus, McGlynn [161] concluded that the $T_1 \rightarrow S_0$ radiationless process is less sensitive to a heavy atom perturbation than the intersystem crossing, but more sensitive than phosphorescence. These assertions are however in contradiction with two other reports [162] [163], which stated that the radiative $T_1 \rightarrow S_0$ transitions are much more sensitive to a heavy atom effect than are the corresponding radiationless transitions.

In general, the detailed mechanism of spin-orbit coupling is not known. The action of paramagnetic substances such as oxygen under pressure are thought to involve electron transfer [164] [165], while charge transfer complexes are commonly

invoked for perturbations by heavy atoms [166]-[170]. Studies of phosphorescence in haloaromatics have shown that intramolecular heavy atom effect does not take place when the halogen is coplanar with the aromatic ring [174]. However, the packing forces of the host lattice used for low temperature experiments very often force the halogen to be slightly nonplanar with the ring and thus allow a spin-orbit interaction [150] [151].

Interestingly, various attempts to establish a relationship between the distance of the heavy atom from the reacting chromophore and the magnitude of the spin-orbit coupling were unfruitful [171] [172].

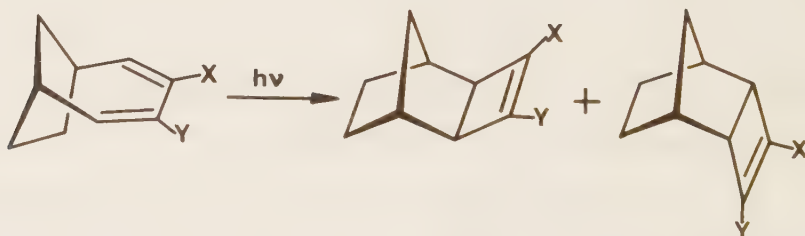
2.2. Direct and sensitized irradiations of bicyclo[4.2.1]nona-2,4-dienes

Solutions of bicyclo[4.2.1]nona-2,4-diene (51) and its mono and dichloro derivatives (45 and 53) in n-hexane were stirred under nitrogen and irradiated by means of an unfiltered medium pressure mercury lamp at 25°. Periodically, the reaction was monitored by vapor phase chromatography. In each experiment, the reaction products consist almost exclusively of the two expected cyclobutene derivatives. These were separated by VPC and analysed by NMR spectroscopy. The essential feature which allows a differentiation between the two isomeric structures is the magnitude of the coupling constant between the bridgehead protons ($^3J_{H1H2}$ and $^3J_{H5H6}$). Thus, a value of

4.5-5.0 Hz is characteristic of an exo disposition of the C2 and C5 protons on the norbornane skeleton [173] [174]. In each case, the exo isomer has the shorter retention time in gas chromatography.

The sensitized irradiations were carried out on identical solutions, but containing acetophenone as sensitizer, and using a filtered medium pressure mercury lamp ($h\nu > 300$ nm). For analytical reasons, the dichloro derivative 53 was irradiated in acetone as solvent and sensitizer. The results of both direct and sensitized irradiations are summarized in table 2.

Table 2



<u>Direct irradiations</u>		<u>exo</u>	<u>endo</u>	<u>% conversion after</u>
				<u>6 hours</u>
<u>51</u>	X=Y=H	<u>54</u> 30%	<u>55</u> 70%	92
<u>45</u>	X=Cl; Y=H	<u>56</u> 53%	<u>57</u> 47%	42
<u>53</u>	X=Y=Cl	<u>58</u> 60%	<u>59</u> 40%	17
<u>Sensitized irradiations</u>				<u>% conversion after</u>
				<u>2½ hours</u>
<u>51</u>	X=Y=H	<u>54</u> 68%	<u>55</u> 32%	5
<u>45</u>	X=Cl; Y=H	<u>56</u> 70%	<u>57</u> 30%	26
<u>53</u>	X=Y=Cl	<u>58</u> 71%	<u>59</u> 29%	47

In both sets of experiments, the percentage ratios observed were invariant with time. As the sensitized irradiations of 51, 45 and 53 all gave almost an identical product distribution (exo/endo: ~70/30), the ratios resulting from the direct irradiations clearly depend on the substituents. Thus, successive introduction of a first and a second halogen into the chromophore results in a remarkable change in the product ratios (exo/endo: 30/70 for the products from compound 51, vs. 60/40 for the products from compound 53).

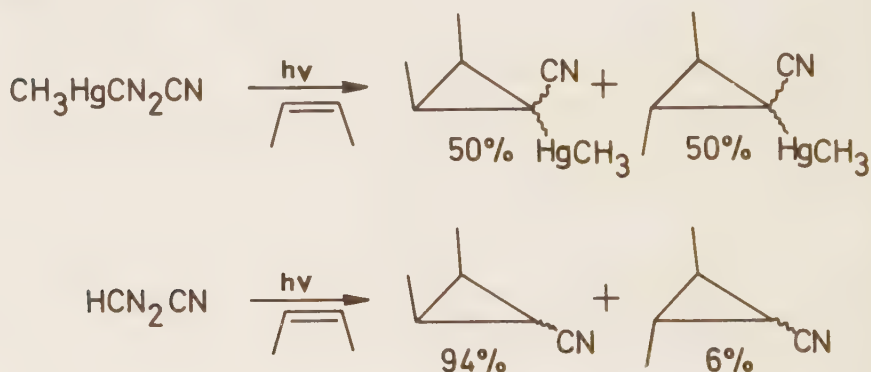
As the formation of polymeric material takes place during the direct irradiation of 53 and during the sensitized irradiation of 51, the percentages of conversion were established after complete disappearance of these starting dienes in both series of experiments respectively.

2.3. Heavy atom effect and product distribution

[2+2] and [4+2] cycloadditions of acenaphthylene with maleic anhydride [175] [176], acrylonitrile [177] and cyclopentadiene [178] have been found to proceed in higher yield, when carried out in halogenated solvents. However, very little has been reported on similar effects on product distribution.

Anastassiou reported a thermochemical heavy atom effect [179]. He found that the insertion of cyanonitrene into C-H bonds of hydrocarbons loses its stereospecificity in dibromomethane, due to the formation of radicals from the triplet ground state of the nitrene.

An intramolecular heavy atom effect has been found in a carbene reaction. Photolysis of diazoacetone nitrile in the presence of *cis*-butene is a highly stereospecific process in that 94% of the *cis*-1,2-dimethylcyclopropane adduct was obtained. Similar photolysis with α -methylmercuridiazacetone nitrile, however, gives a roughly 1:1 mixture of both *cis* and *trans* cyclopropane adducts.[180]



The α -mercuric group greatly accelerates the intersystem crossing to the triplet ground state of the carbene. The high stereospecificity observed in the cyanocarbene addition to *cis*-2-butene is therefore completely lost.

In photodimerization of olefins such as coumarin [181] [182] or acenaphthylene [183]-[187], intermolecular heavy atom effects were found to affect the product distribution (table 3).

In view of the known reluctance of conjugated dienes to undergo intersystem crossing in the excited state, the product distribution from direct irradiation of compound 51 arises most likely from a ring closure in the singlet excited state.

Table 3



<u>Solvent</u>	<u>% cis</u>	<u>% trans</u>
Cyclohexane	83.2	16.8
"- + 10% EtI	20.2	79.8

It is seen from table 2 that the singlet excited state of the diene 51 led to the preponderant formation of the endo-cyclobutene derivative 55. On the other hand, the triplet excited state gave mainly the exo isomer 54. The energy difference between singlet and triplet excited states is probably responsible for these different product ratios.

According to expectation, introduction of such heavy substituents in 45 and 53 enhances the $S_1 \rightarrow T_1$ intersystem crossing. Consequently, the resulting product ratios should resemble more and more those found in the sensitized experiments. This hypothesis is indeed confirmed, since the exo/endo ratio (60/40) of 58 and 59 arising from direct irradiation of the dichloro derivative 53 is very similar to that obtained from the sensitized reaction (71/29).

Thus, the photoisomerizations of 51, 45 and 53 appeared to be the first case of an intramolecular heavy atom perturbation in a conjugated diene, which has a directive effect on the product distribution.

3. Reductive dehalogenation of bicyclic halides

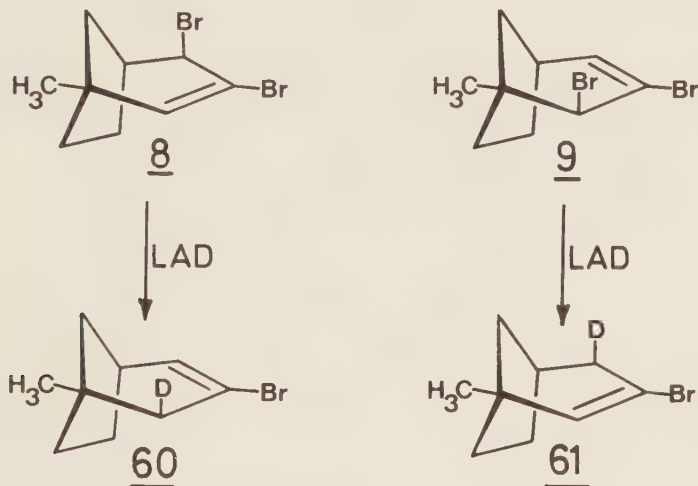
3.1. Metal hydride reductions

3.1.1. Reactivity of allylic halides

The satisfactory exploitation of cycloadditions with dichlorocarbene as a synthetic method depends largely on how easily the resulting product can be chemically modified. One of these problems concerns the removal of chlorine and its replacement by hydrogen. Reductive removal of allylic chlorine presents no difficulty and is smoothly effected with complex metal hydrides such as lithium aluminium hydride [89], sodium borohydride [188] or even tri-n-butyltin hydride [189]. However, as each of these reagents reacts according to a particular mechanism, the choice of reagent strongly depends on the expected reaction course. While aluminium hydrides are known to undergo S_N2 type reactions [190], tri-n-butyltin hydride reductions are thought to involve radical intermediates [92] [189]. Moreover, migration of the double bond is not an uncommon phenomenon during these reductions. Thus, although primary allylic halides are reduced by lithium aluminium hydride (LAH) without double bond migration [191] [192], reduction of secondary allylic halides proceeds mainly with allylic rearrangement [193]. The reason suggested is a greater steric impediment for the approach of the reagent to a secondary than a primary allylic center [194].

Amongst the possible mechanisms involving allylic rear-

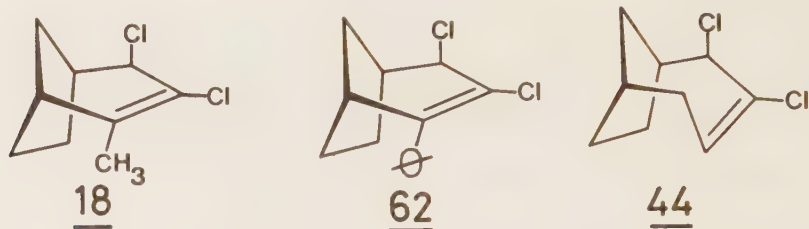
rangement, S_N2' is one of the most difficult to demonstrate unambiguously [193]. Thus, one of the first attempts in the bicyclic series concerns the reductive dehalogenation of an equilibrium mixture of 1-methylbicyclo[3.2.1]octenyl bromides with lithium aluminium deuteride (LAD) [196].



An 80:20 mixture of 8 and 9 on treatment with an excess LAD gave the deuterated derivatives 60 and 61 in a 84:16 ratio. These results were interpreted at the time in terms of an exclusive S_N2' process. However, as both starting bromides proved impossible to separate, a definitive interpretation of the mechanism operating could not be made.

In order to further investigate this mechanistic problem, 2-methyl- and 2-phenylbicyclo[3.2.1]octenyl chlorides 18 and 62 have been selected, as both are isolated as single isomers. Similarly to 8 and 9, compounds 18 and 62 possess their cyclohexenyl moieties in the half-chair conformation and exhibit

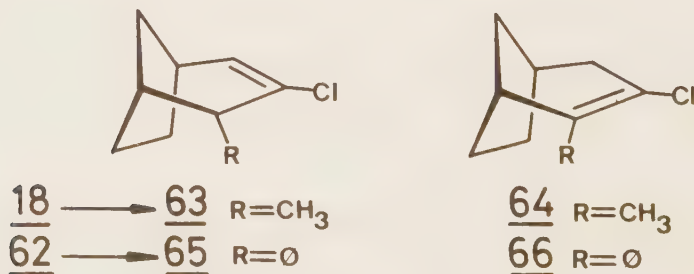
also a stereospecific reactivity on their exo sides [197].



Lastly, these reductions were also carried out on the higher unsubstituted homologue 44 to test the extent of the conformational requirement.

3.1.2. Lithium aluminium hydride

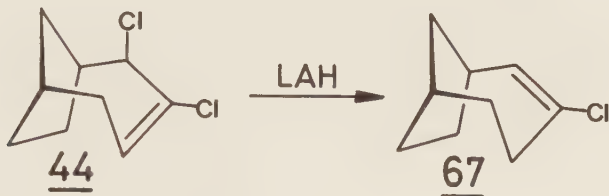
Treatment of 18 with lithium aluminium hydride in boiling ether afforded an 80:20 mixture of the two reduction products in 73% yield. Separation by vapor phase chromatography and identification gave 3-chloro-endo-2-methylbicyclo[3.2.1]oct-3-ene (63) and 3-chloro-2-methylbicyclo[3.2.1]oct-2-ene (64).



Both isomers (63 and 64) were tested separately and found to be stable under the reaction conditions. Both isomers were also stable under basic conditions (sodium methoxide, at 135°).

Similar reduction of the phenyl substituted derivative 62 yielded the two isomers 65 and 66, but in a 45:55 percentage ratio.

On the other hand, treatment of exo-3,4-dichlorobicyclo-[4.2.1]non-3-ene (44) with an excess LAH in boiling ether for 48 hours gave exclusively the rearranged product 67 in 76% yield.



This last result shows that the reduction course of the constrained cycloheptenyl chloride 44 is not identical to that of the conformationally constrained cyclohexenyl halides. A unique mechanism seems to operate in this particular case.

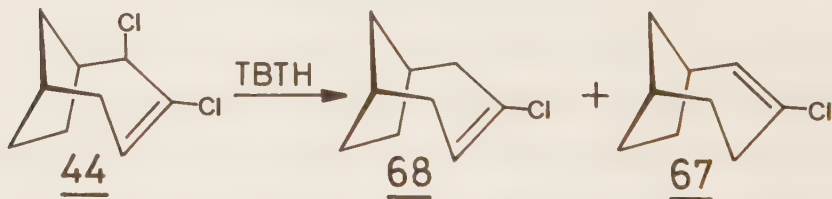
Reductions of the tri- and tetrachloro derivatives 46 and 48 gave complex mixtures resulting from adventitious reduction of vinylic chlorines.

3.1.3. Tri-n-butyltin hydride and sodium borohydride

In order to know to what extent the nature of the reagent can affect the product distribution, both chlorides 18 and 62 were treated with tri-n-butyltin hydride (TBTH). TBTH reductions are thought to proceed by a radical mechanism. It follows that the product distribution from 18 and 62 should provide a new indication regarding the nature of the LAH reductions.

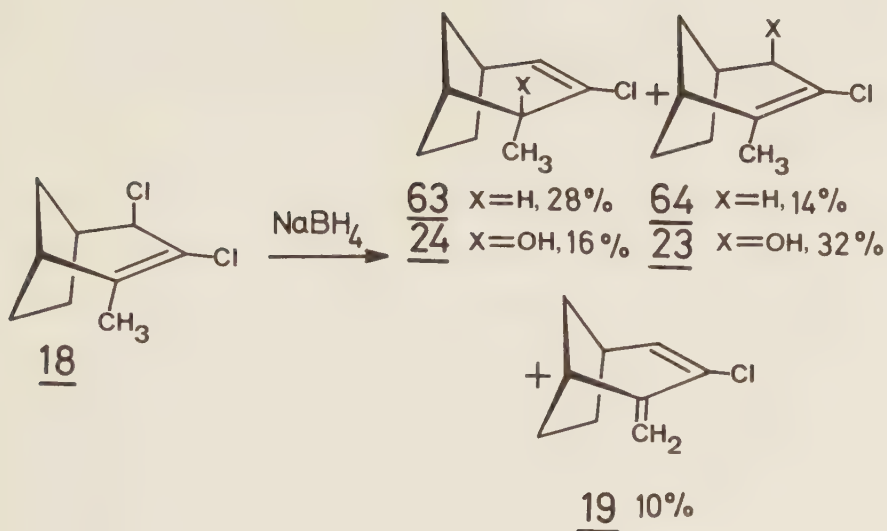
Stirring and heating exo-3,4-dichloro-2-methylbicyclo-[3.2.1]oct-2-ene (18) without solvent and with an excess tri-n-butyltin hydride at 80° for 24 hours gave rise to the formation of 63 and 64 in the ratio 20:80. Surprisingly, this ratio is the reverse of that found in the LAH reduction. The phenyl derivative 62 reacted similarly with TBTH to yield mainly the unrearranged product 66.

In contrast to the LAH reduction, the action of TBTH on 44 produced the allylically unrearranged product 68 together with 67 in a ratio of 80:20.



Finally, as a check for a hypothetical formation of ionized intermediates in the reactions with lithium aluminium hydride, reduction of 18 was further investigated in a more ionizing medium. On treatment with sodium borohydride in 80% aqueous diglyme, a mixture of products resulting from both reduction and hydrolysis of 18 was obtained.

The formation of the isomeric alcohols 23 and 24 and the diene 19, in addition to the expected reduction products 63 and 64, clearly demonstrates the intermediacy of an allylic cation or at least of its ion pair.



3.1.4. Mechanistic conclusions

Despite the amount of information now available, a clean-cut mechanistic interpretation of these LAH reductions is still difficult to make. Previous experiments have established that the reduction of the bicyclooctenyl halides with lithium aluminium deuteride takes place in a synfacial manner, which implies necessarily a 100% allylic rearrangement [198]-[200]. Two possible and closely related mechanisms can account for a synfacial displacement, $\text{S}_{\text{N}}2'$ and $\text{S}_{\text{N}}\text{i}'$. The $\text{S}_{\text{N}}2'$ designation applies to a reaction in which little or no interaction exists between the entering and leaving groups. On the other hand, in a $\text{S}_{\text{N}}\text{i}'$ reaction, the interaction between these two groups may be so large that the transition state can be quasi-cyclic (see figure 10) [198].

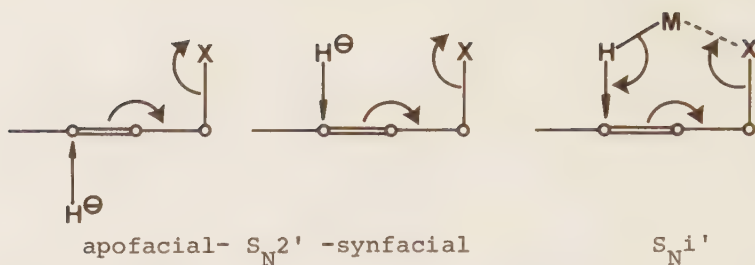


Figure 10

Both processes can operate on either a covalent species or an ion pair. In the event of the reactive allylic chlorides 18, 62 and 44, the covalent species would lead exclusively to the rearranged products. As it has been demonstrated that neither S_N2 nor isomerization processes take place under the reduction conditions, they can be definitely discarded.

The formation of ion pairs, however, may account for the observed product distribution. According to Sneen [201], intimate ion pairs and solvent separated ion pairs exist as discrete reactive intermediates.



Figure 11

The positive charge in the intimate ion pair is still localized on the allylic carbon to which the counteranion is closely associated (see figure 11). Therefore, attack of a free or complex hydride in an S_N2' fashion should lead mainly, or even

exclusively, to the rearranged product. In the solvent separated ion pair, however, charge delocalization is effective and the nucleophilic attack takes place on both allylic carbons in an S_N2' or S_N1' processes to give two isomers. Understandably, preponderant attack occurs on the tertiary cationic center.

Considering the substituent effects, electron donating groups cause probably more allylic delocalization and so induce the formation of solvent separated ion pairs. This interpretation accounts reasonably well for the behaviour of compounds 18 and 44. In the reductive dehalogenation of 62, however, an additional factor has to be considered. The double bond in conjugation with the phenyl group in the unrearranged product from 62 increases its thermodynamic stability and explains its importance in the reaction mixture.

Further support for a mechanism involving ion pairs is provided by the sodium borohydride reduction of 18. The ionizing medium used should give rise to a competition between the two different nucleophiles, hydride and water [202]. It has been shown, that in solvolytic conditions, the less stable the carbonium is the more reactive and the least selective towards agents of different nucleophilicity [203]. Thus, in the present case, the amount of rearranged product formed should exceed that of the unrearranged one. Indeed this was observed.

Finally, the reverse ratio found for the reductions with TBTH proves to be of little value for the study of alumino-

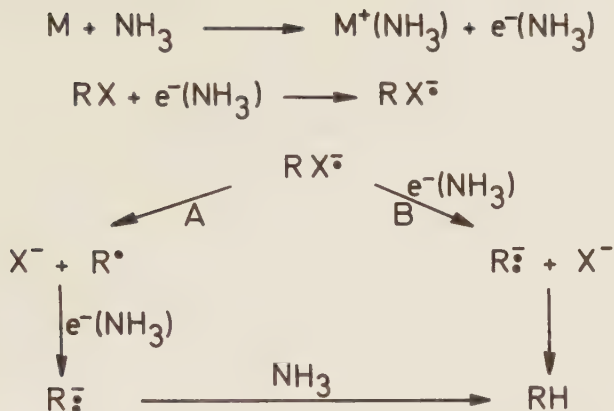
hydride reductions. Even if the macroscopic chemical behavior of both reagents is the same, the mechanism involving ion pairs cannot be easily related to homolytic pathways [204].

3.2. Dissolving metal reductions

3.2.1. Reductive cleavage of both allylic and vinylic carbon-halogen bonds

It has been known for a long time that dissolving metals effect the reduction of a wide variety of organic compounds [205]. In particular, the action of alkali metals undergoing solution in liquid ammonia are useful for bringing about reductive dehalogenation of vinyl and bridgehead halides (Birch reductions) [206] - [208]. The incorporation of ether, tetrahydrofuran or 1,2-dimethoxyethane as co-solvents often increases yields of reduced products by virtue of the resulting increased solubility of the organic substrate .

The mechanism involved in these reductions is still not known for certain [209]. One interpretation is that they may be considered as internal electrolytic reductions, in which an electron from the metal is transferred in a solvent cage to the organic molecule. The resulting radical anion can then acquire a second electron to give the anion, which then accepts a proton from the solvent. Alternatively, the radical anion could lose an anion to give a new radical, which in turn also acquires a second electron from the reducing medium to give the same anion. These processes are illustrated below.

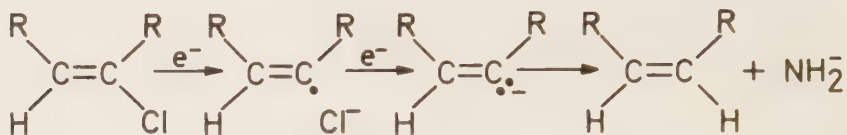


When an optically active halide RX is used, the resulting hydrocarbon is one in which the original configuration is retained [210]. However, no unambiguous evidence for the radical route (A) [209] [211] or the carbanion process (B) [212]-[214] has been found. It was shown later that the two mechanisms should be dependent on the reaction conditions [215]. Thus, while racemization should result from a rapidly inverting radical intermediate, retention of configuration would be expected from a carbanion species. Experimentally, it has been demonstrated that retention of optical activity in the products is the greatest when the metal concentration, the carbon-halogen bond strength and the solubility of the starting material are the highest.

Another point of mechanistic interest is that the reduction of vinyl halides takes place without any geometric or ZE isomerization [216].

Once again, the dissolving metal furnishes an electron to the carbon which is attached to the halogen atom which sub-

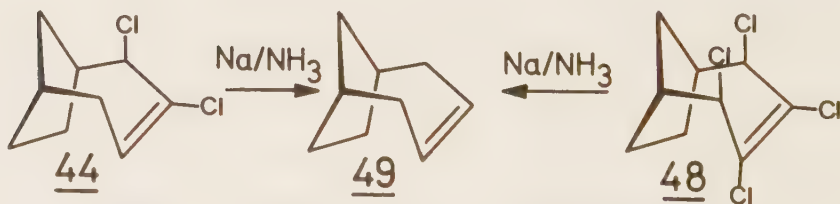
sequently cleaves to give halide and the vinyl radical [217].



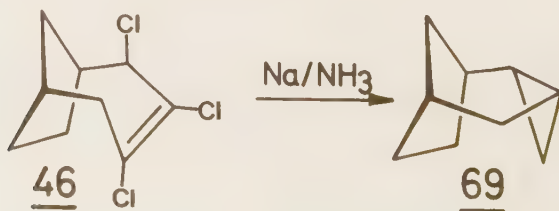
The addition of a second electron furnishes the appropriate vinyl carbanion, which retains its configuration and subsequently accepts a proton from the medium to give the olefin of unchanged configuration.

3.2.2. Expected and unexpected reaction courses

Dichloro and tetrachloro derivatives 44 and 48 behave normally towards an excess of sodium in liquid ammonia giving the expected olefin 49 in 68% and 31% yield respectively.

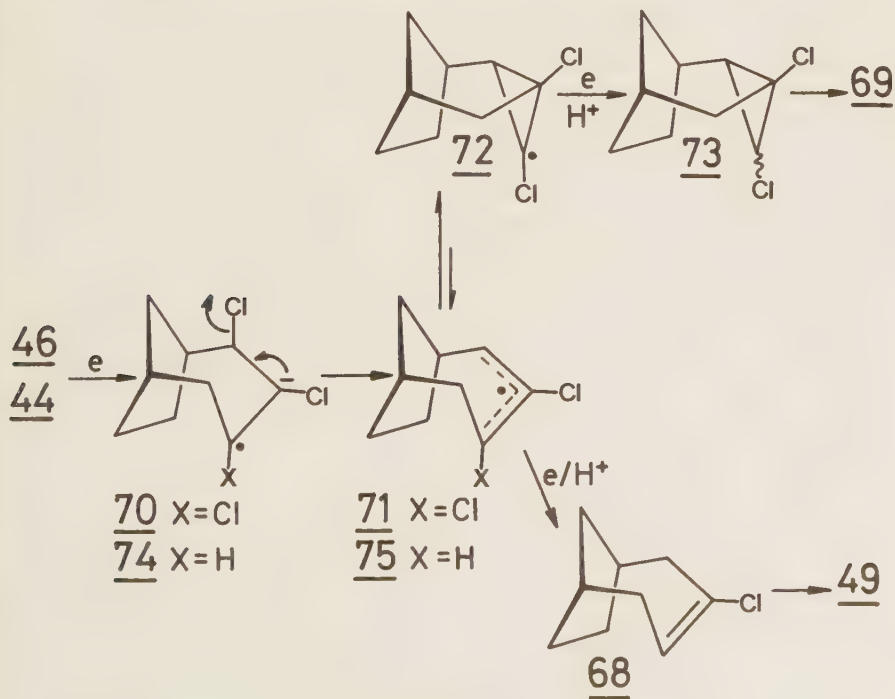


Surprisingly, treatment of the trichloro compound 46 under Birch conditions gives none of the olefin 49, but instead endo-tricyclo[4.2.1.0^{2,4}]nonane (69).



This unusual ring closure proved to be reproducible and 69 was isolated and purified by sublimation in 55% yield.

It is difficult to explain unequivocally the course of this surprising reaction. Under the conditions used, it seems reasonable to invoke either a radical or a carbanion intermediate as the precursor of the three-membered ring. However, an intramolecular nucleophilic displacement of a β -halogen by a carbanion is geometrically unfeasible in these systems, as the ring prevents Walden inversion. Therefore, it is ruled out. Thus, the addition of one electron to the double bond yields presumably a radical anion (70). Internal displacement of the α -chloro substituent gives a stable delocalized radical (71).



Then, electrocyclic closure of the allyl radical 71 into the cyclopropyl radical 72 may be possible. Afterwards, 72 accepts a further electron and proton to form the dichlorocyclopropane derivative 73, which on reductive cleavage of both carbon-halogen bonds yields 69.

Application of this hypothetical mechanism to the dichloro compound 44 leads to the allyl radical 75. In all probability, this intermediate does not undergo ring closure, but rather gives on further reduction the parent olefin 49. The question now arises as to whether the second halogen in 71 is responsible for this cyclization or better, whether the monochloro radical 75 is really an intermediate.

To our knowledge, nothing yet has been reported on similar electrocyclic closures of an allyl radical into a cyclopropyl radical. The reverse process, however, has been the object of much theoretical work. Although previous reports predicted a cyclopropyl-allyl radical transposition in a conrotatory fashion [132] [133], recent calculations indicated that a disrotatory process would be slightly preferred [218] [219]. The activation energy for the opening of a cyclopropyl radical following a disrotatory process was found to be c.a. 30 Kcal/mole, whereas a conrotatory mode would require c.a. 44 Kcal/mole [220]. Experimentally, Sustmann and Rüchardt [221] investigated the ring opening of substituted cyclopropyl radicals and decided in favor of a disrotatory process.

Cyclopropyl radicals are thought to be almost as stable

as allyl radicals [222]. The ESR spectrum of the 2,3,3,3-tetramethylcyclopropyl radical in the range of -48° to -108° did not show any ring opening [223].

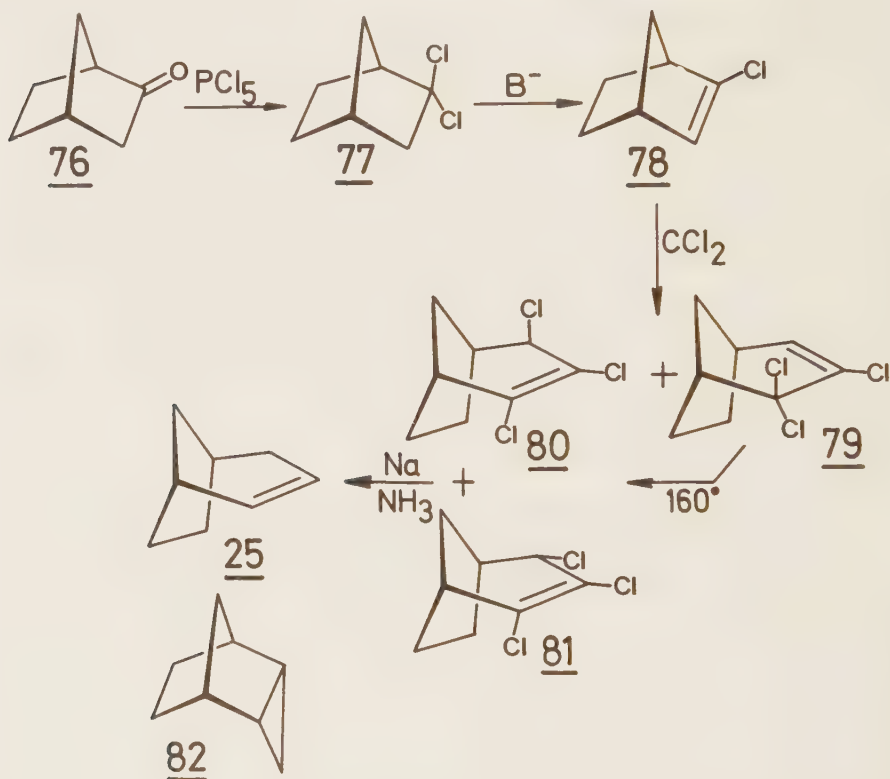
According to the above calculations [220], the electrocyclization of 71 would require an activation energy of at least 30 kcal/mole, which would not be accessible under the reduction conditions. These energetic considerations do not support the hypothesis of the ring closure. Therefore, the presence of the chloro substituents is expected to have a direct effect on the course of these reductions.

3.2.3. Scope of the retro-cyclopropyl-allyl transpositions: ring strain effects in the bicyclic series

The unusual course followed by the Birch reduction of exo-2,3,4-trichlorobicyclo[4.2.1]non-3-ene (46) led us to wonder whether this reactivity could be more general and applicable to other 1,2,3-trichloro allyl systems. In order to further investigate this electrocyclic closure, we selected both the lower and higher homologues of 46 as starting substrates. Finally, we extended this study to one example in the monocyclic series.

Treatment of norcamphor (76) with phosphorus pentachloride gives the gem-dichloro derivative 77 in 76% yield [224]. This compound is dehydrochlorinated by means of potassium *t*-butoxide in dimethylformamide to yield 78 (78%) [113]. Dichlorocarbene addition to 2-chloronorborn-2-ene (78) produces a mixture of 79 and 80 (68%) in the ratio 1:2. Heating of this mixture at 160° under nitrogen for ninety minutes results in

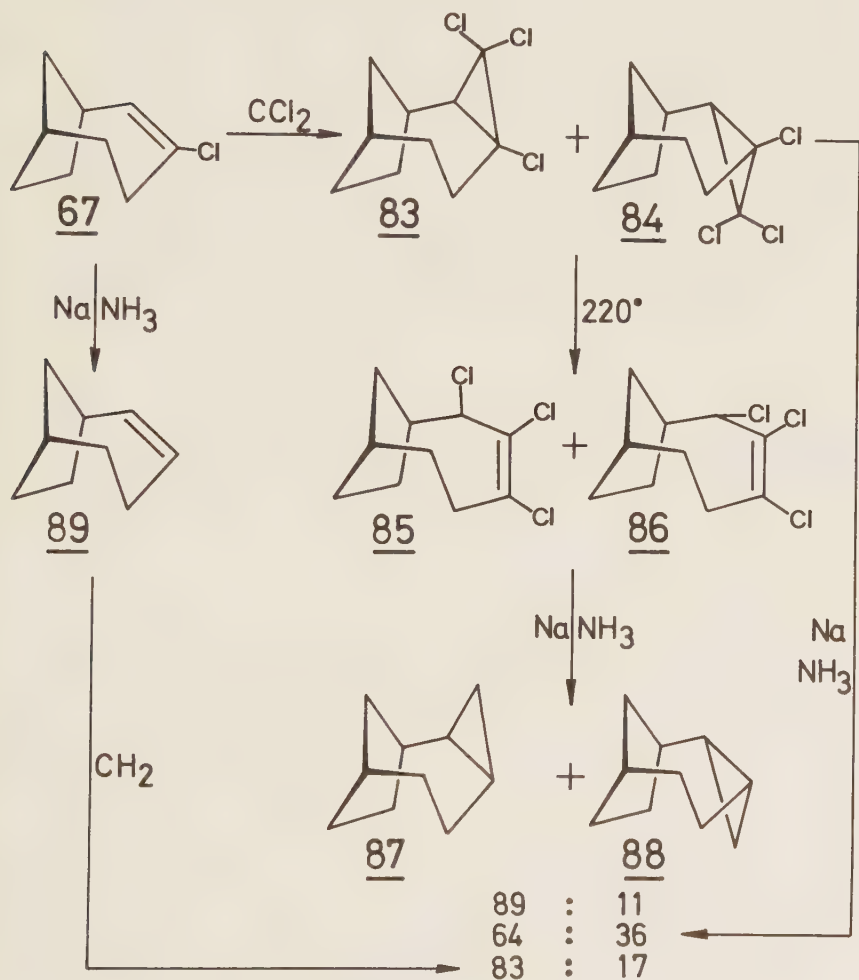
the complete conversion of 79 into the thermodynamically more stable isomers 80 (91%) and 81 (9%).



The reductive dehalogenation of 80 and 81 with sodium in liquid ammonia does not yield the expected tricyclic compound 82, but only the parent olefin 25. As a large increase in strain would have been introduced into the molecule for such an allyl-cyclopropyl transposition, it is concluded that the intermediate allyl-cyclopropyl equilibrium is completely displaced on the side of the allyl species. The latter is then further reduced to give the olefin 25.

The correctness of this steric argument was checked by

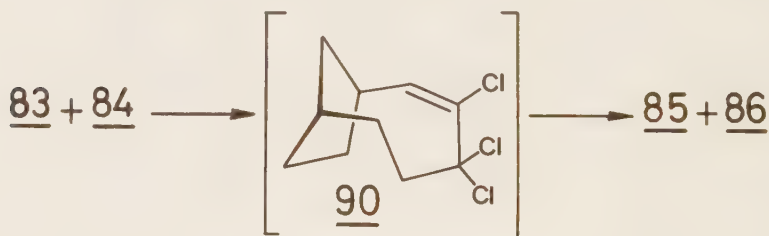
carrying out the reduction of the next higher homologue of 46, namely 2,3,4-trichlorobicyclo [5.2.1] dec-3-ene. The synthesis of the latter compound was achieved by the reaction of dichlorocarbene with 3-chlorobicyclo [4.2.1] non-2-ene (67).



The addition reaction proceeds in 76% yield and gives both the exo and endo adducts (83 and 84) in the ratio 86:14. An

interesting point here concerns the absence of the remarkable stereospecificity which is always observed in the carbene additions to bicyclo[2.2.1]heptene and bicyclo[3.2.1]octene systems.

The thermal cyclopropyl-allyl rearrangement at 220° of the mixture of 83 and 84 gives exo- and endo-2,3,4-trichlorobicyclo[5.2.1]dec-3-ene (85 and 86) in the ratio 54:46. A mechanism involving a fully concerted rearrangement [81] [97] implies the formation of the short-lived kinetic product 90, which on further heating undergoes [1,3]migrations of chlorine to yield an epimeric mixture of 85 and 86.

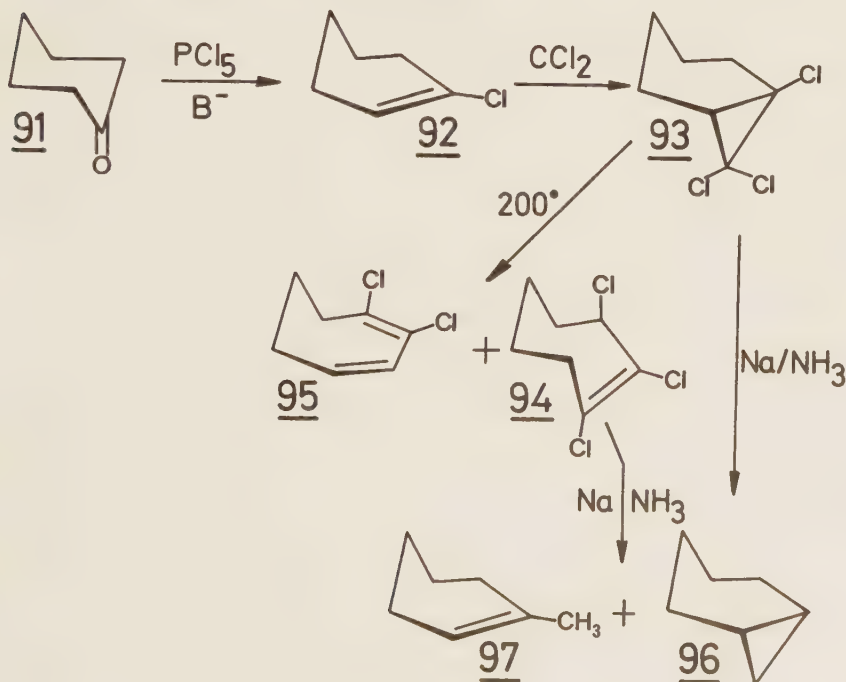


On treatment with sodium in liquid ammonia, 85 and 86 give two isomeric cyclopropyl hydrocarbons (87 and 88) in the ratio 89:11 in a total yield of 35%. The reaction is accompanied by the formation of polymeric material. Both isomers prove difficult to separate, even by vapor phase chromatography. The exo and endo structures were assigned to 87 and 88 respectively on the basis of a chemical evidence. Addition of methylene to the unsymmetrical olefin 89 produces a mixture of two cyclopropane derivatives, in a ratio (83:17), which is very similar to that found for 83 and 84 (86:14) [225]-[227]. The retention times of these cyclopropane compounds on GLC

correspond to those of 87 and 88 respectively. Further support for structures 87 and 88 is provided by the reductive dehalogenation of a mixture of 83 and 84, which gives the same hydrocarbons, but in a different ratio (64:36).

3.2.4. Trichlorocycloheptene: an example in a monocyclic system

To test further the generality of this electrocyclic ring closure, 1,2,3-trichlorocycloheptene (94) was chosen. Synthesis of this substrate starts from cyclohexanone (91).



Chlorination and dehydrochlorination yields 1-chlorocyclohexene (92). Addition of dichlorocarbene to 92 affords the expected

ted adduct 93, which on heating to 200° gives the product of rearrangement 94, accompanied by some of the product in which elimination has occurred (95). The yields of 94 and 95 were 41% and 59% respectively.

Reductive dechlorination of 94 under Birch conditions gives a mixture of norcarane (96) and 1-methylcyclohexene (97) in 17% and 14% respectively. Both isomers were isolated by preparative GLC and identified by spectral methods [228] [229].

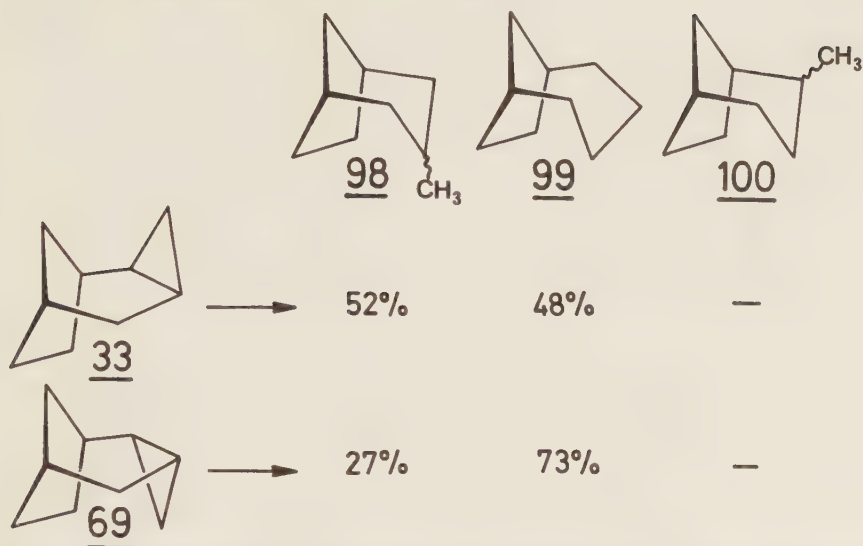
3.2.5. Structure determination of the cyclopropane derivatives

endo-Tricyclo[4.2.1.0^{2,4}]nonane (69), obtained from the Birch reduction of exo-2,3,4-trichlorobicyclo[4.2.1]non-3-ene (46), was identified by comparing its ¹³C NMR spectrum with that of the exo isomer 33. Further chemical evidence for both cyclopropane structures is provided by hydrogenolysis of 33 and 69 and examination of the products formed [227].

Analysis of both reaction mixtures by vapor phase chromatography indicates the presence of two compounds having identical retention times, but in different ratios (see table 4). The two components were separated by VPC and identified by NMR and MS. One of these components was shown to be bicyclo[4.2.1]nonane (99) and the other was found to be 3-methylbicyclo[3.2.1]octane (98), a single isomer of unknown configuration at C3. None of the 2-methyl isomers was detected.

Apart from the proof of structure of the endo hydrocar-

Table 4: Hydrogenolyses of 33 and 69



bon 69, these findings provide an interesting test of the mechanism proposed by Irwin to explain the hydrogenation of the cyclopropane ring [231]. He maintains that the product distribution depends on both electronic and steric effects of the cyclopropane substituents. As the electronic effects of the host bicycles in 33 and 69 are expected to be very similar, the three-membered ring opening will be mainly sterically controlled, as the bond to be broken approaches the catalyst surface. In principle, the cyclopropane can open in three separate ways (see figure 12). Consequently, for opening modes (a) and (c), compounds 33 and 69 should exhibit almost identical reactivity. On the other hand, opening mode (b) should be more sensitive to a steric interaction between the ethylene bridge and the metal surface in the hydrogenolysis of 33 than between the methylene bridge and the catalyst surface in the reaction

involving compound 69 (see figure 12).

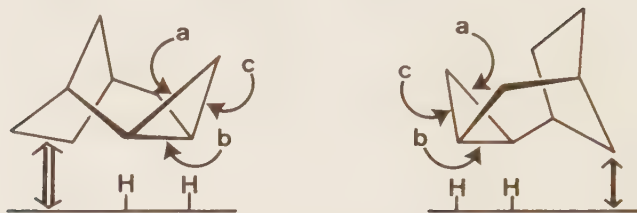


Figure 12

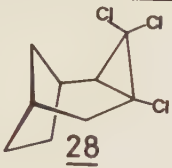
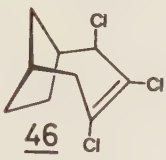
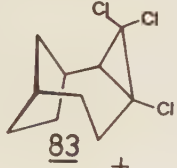
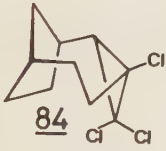
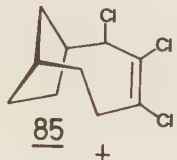
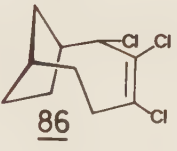
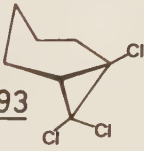
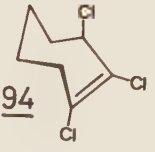
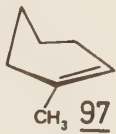
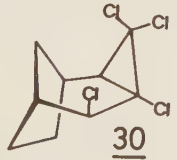
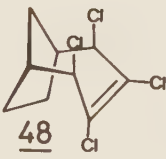
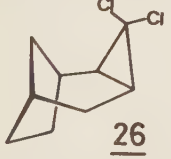
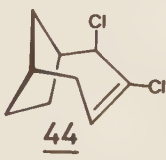
The relatively large formation of compound 99 (48%) from the disfavoured opening mode (b) of 33 illustrates the difference in reactivity between internal and external bonds in these three-membered ring systems. The fact that none of the isomer 100 was detected indicates that one external bond is unexpectedly much stronger than the other.

Cleavage of the external bonds according to mode (a) gives 3-methylbicyclo[3.2.1]octane skeletons with their cyclohexane moieties in the chair conformations. Opening of the exo derivative 33 should lead to an equatorial methyl substituent in 98. Similarly, the formation of a methyl group in the axial configuration is expected from compound 69. The yields obtained experimentally, 52% and 27% respectively, may also reflect the relative stabilities of the methyl groups in both configurations.

3.2.6. Tentative mechanistic interpretation

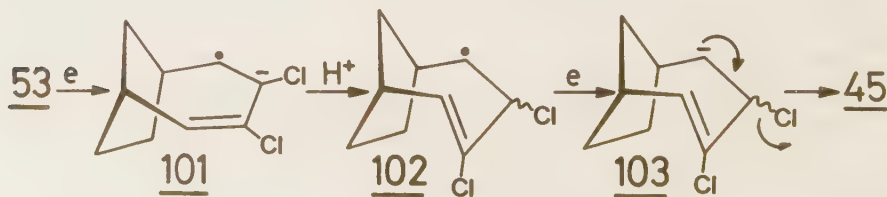
Although the detailed mechanism of these reductive dehalogenations cannot be established rigorously, some interesting observations can be made from the data presented in table 5:

Table 5

DICHLOROCARBENE ADDUCT	RING OPENING		DEHALOGENATION	
	PRODUCT	YIELD(%)	PRODUCT	YIELD(%)
 <u>28</u>	 <u>46</u>	76	 <u>69</u>	55
 <u>83</u> +  <u>84</u>	 <u>85</u> +  <u>86</u>	80	 <u>87</u> +  <u>88</u>	35
 <u>93</u>	 <u>94</u>	41	 <u>96</u>  CH ₃ <u>97</u>	30
 <u>30</u>	 <u>48</u>	47	 <u>49</u>	31
 <u>26</u>	 <u>44</u>	47	 <u>49</u>	68

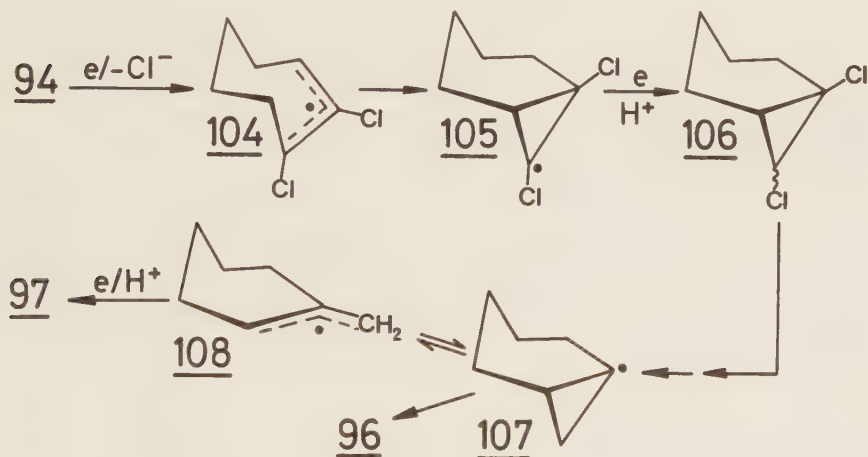
Surprisingly, among all the compounds investigated, those which are liable to lose hydrogen chloride (44 and 48) give mainly the parent olefins under the Birch conditions. This ability to form the conjugated diene is well illustrated by the poor yields (41-47%) obtained for the cyclopropyl-allyl rearrangements of their corresponding gem-dichlorocyclopropane precursors (26 and 30). This eventually means that a dehydrochlorination takes place under the Birch conditions. Then usual reduction of the resulting conjugated diene leads to the mono-olefin 49 (see section 1.3.4.).

What appears difficult to explain is the behaviour of the diene 53. On treatment with sodium in liquid ammonia, it gives exclusively the olefin 49 in a good yield (60%). As a 1,4-addition of an electron and then capture of a proton should yield the allyl radical 71, ring closure to the cyclopropane derivative 72 is expected. Considering the properties of similarly halogenated dienes [232], it would appear that they are usually unreactive in the diene syntheses. It follows that the introduction of a second halogen in the conjugated system destroys some of its diene character. The system behaves more like an isolated double bond in the first step.



Thus, addition of one electron to 53 gives the radical anion 101, which on capture of a proton produces the homoallyl radical 102. Addition of a second electron and displacement of the allylic chlorine leads to the known monochloro diene 45.

In the reductive dehalogenation of the monocyclic system 94, the mechanism appears even more complex, as both reaction products probably arise from a three-membered ring intermediate. By analogy with the mechanism proposed in the bicyclic series, it seems plausible to consider the following route.

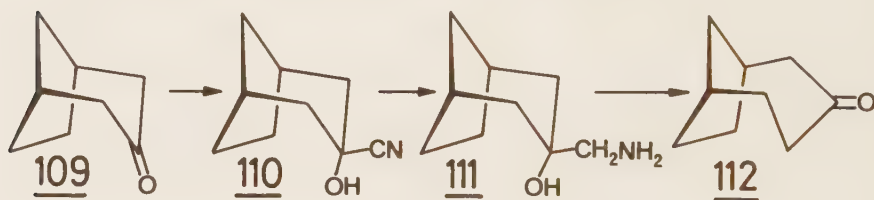


The formation of 1-methylcyclohexene (97) can be explained as involving a cyclopropyl-allyl equilibrium between radicals 107 and 108 in competition with the formation of norcarane (96). From a thermodynamic point of view, the overall reaction leading to 97 corresponds to the conversion of a cycloheptene system to the more stable isomeric methylcyclohexene skeleton [102]. In the bicyclic series, however, the presence of the bridge prevents such a ring contraction.

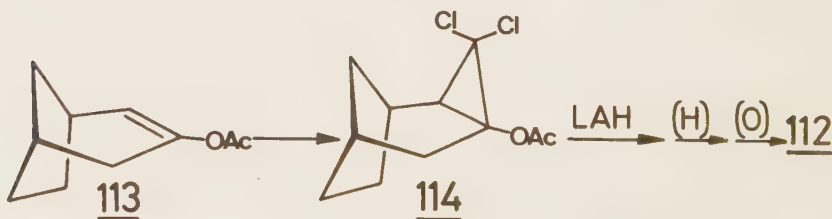
4. SYNTHESIS OF BICYCLO[4.2.1]NONAN-3-ONE

4.1. The choice of the starting material

Several syntheses of bicyclo[4.2.1]nonan-3-one (112) have been already reported. Thus, addition of diazomethane to bicyclo[3.2.1]octan-3-one (109) gives a difficultly separable mixture of bicyclo[4.2.1]nonanones-2 and -3 [233]. The Tiffeneau ring enlargement of the semi-pinacol 111, derived from 109 via hydrogenation of 110, gives the keton 112 [234] [235].



Addition of dichlorocarbene to the enol acetate of 109 and subsequent modifications of the resulting adduct (114) is also effective [236].

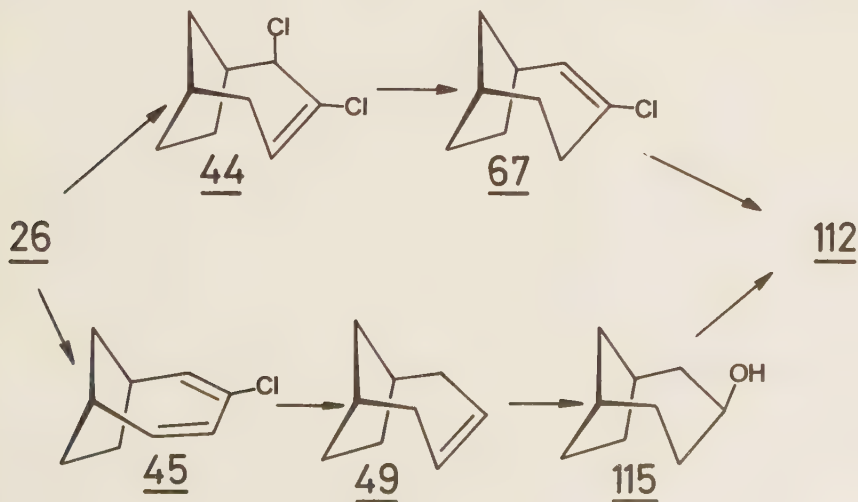


The disadvantage common to all these synthetic routes rests in the fact that they start from the rather expensive bicyclo[3.2.1]octan-3-one (109). Moreover, in most cases, the resulting ketone 112 has to be further purified by recrystallization of its semicarbazone .

Finally, the use of dihalocarbenes for the ring enlargement of more accessible bicyclo[3.2.1]octene derivatives has been investigated [237] [238]. While addition of dichlorocarbene to exo-3,4-dichlorobicyclo[3.2.1]oct-2-ene (29) and rearrangement of the resulting adduct (30) are inefficient, the same reaction carried out on the monochloro olefin 27 proves promising. Unfortunately, the subsequent reductions of the trichloro derivative 46 do not proceed as expected (see section 1.3. and 3.2.). Finally, the parent olefin 25 appears to be the substrate of choice in this synthesis.

4.2. The carbene route: an improved method

Bicyclo[3.2.1]oct-2-ene (25) is easily prepared from the commercially available 5-hydroxymethylnorborn-2-ene [239]. Addition of dichlorocarbene to 25 proceeds smoothly and gives the tricyclic adduct 26 in 94% yield.



The conventional route involving thermal ring opening (26---->44), removal of the allylic chlorine by LAH reduction (44---->67) followed by acid hydrolysis of the vinyl chloride (67---->112), gives 47%, 76% and 28% yield respectively.

However, the olefin 49 has been prepared already from 26 by making the rearrangement occur with elimination of HCl (26---->45) (63%) (see section 1.3.4.). It appears therefore feasible to prepare the ketone 112 by hydroboration [240] [241] of 49, followed by oxidation [242] of what seems to be *exo*-3-hydroxybicyclo[4.2.1]nonane (115). These last two steps proceed in 70% and 81% yield respectively. Thus, starting from 5-hydroxymethylnorborn-2-ene, ketone 112 can be obtained in an overall yield of 20%, which compares favorably with the yields of 17% and 18%, starting from norbornene by the methods of Kraus [236] and Hartmann [234] [235].

* * *

EXPERIMENTAL PART

Gas liquid chromatography (GLC) was carried out on a model F11 (analytical) or model 990 (semi-preparative) or model F21 (preparative) Perkin-Elmer instruments.

IR. spectra were recorded, as films on NaCl plates, on a model 257 Perkin-Elmer spectrometer. UV. spectra were recorded on a model 402 Perkin-Elmer spectrophotometer.

NMR. spectra were determined at 60 MHz on a model R-12 Perkin-Elmer instrument and at 100 MHz on a model XL-100 Va-riant spectrometer using carbon tetrachloride as solvent. Chemical shifts are expressed as ppm with reference to tetramethylsilane taken as zero. Signals intensities are reported in proton units (1H, 2H, etc.); multiplicities are expressed as singlet (s), doublet (d), triplet (t) and multiplet (m).

All boiling and melting points are uncorrected. Mass spectra were performed by Mrs. F. Kloeti and the microanalyses by Dr. K. Eder, Ecole de Chimie, Genève.

The usual work up of a reaction mixture consisted of dilution with water and three extractions with ether. The combined ethereal fractions were washed with water (three times), with a saturated sodium bicarbonate solution (or a 10% aqueous HCl solution, depending on the pH of the reaction mixture), then again with water and finally with a saturated sodium chloride solution. The organic layer was dried over sodium or magnesium sulfate and solvent was removed under reduced pressure.

1. SYNTHESIS OF BICYCLO[3.2.1]OCTENE AND BICYCLO[4.2.1]NONENE

DERIVATIVES

1.1. Bicyclo[3.2.1]octene derivatives

1.1.1. Addition of dichlorocarbene to 2-methylnorborn-2-ene

A mixture of 13 (10.8 g; 0.1 mole), chloroform (12.0 g; 0.1 mole), 50% aqueous sodium hydroxide solution (20 ml) and triethylbenzylammonium chloride (0.4 g) was heated and stirred at 40° for 24 h. The mixture was diluted with water and then extracted with ether. The ether layer was separated and washed with water three times, once with a dilute sodium bicarbonate solution, again with water, and finally with a saturated sodium chloride solution. The ether solution was dried over sodium sulfate and subsequently evaporated. The residual oil was fractionally distilled in vacuo to afford 3-chloro-2-methylenebicyclo[3.2.1]oct-3-ene (19) (1.55 g; 0.01 mole) 10%, and exo-3,4-dichloro-2-methylbicyclo[3.2.1]oct-2-ene (18) (9.7 g; 0.051 mole) 51%.

3-chloro-2-methylenebicyclo[3.2.1]oct-3-ene (19).-B.p. 41-42°/0.15 Torr. UV. spectrum: λ_{max} . (in cyclohexane) 242 nm ($\epsilon = 21300$). IR. spectrum: max. at 3095(w), 3045(w), 1639(w), 1587(m) 890(s), 885(s) and 667(m) cm^{-1} characteristic of the diene and the C-Cl bond.

$\text{C}_9\text{H}_{11}\text{Cl}$ (154.64)	Calc. C 69.92	H 7.17	Cl 22.93%
	Found 69.80	7.13	23.22%

exo-3,4-dichloro-2-methylbicyclo[3.2.1]oct-2-ene (18).-B.p. 66-67°/0.1 Torr. IR. spectrum: max. at 1647(m) and 658(m) cm^{-1} characteristic of the tetrasubstituted double bond and the C-Cl bond.

$\text{C}_9\text{H}_{12}\text{Cl}_2$ (191.10)	Calc. C 56.55	H 6.33	Cl 37.12%
	Found 57.61	6.69	34.01%

A small amount of adduct formed from traces of 2-methylenenorbornane present as impurity was also isolated. The origin of this olefin is the base catalysed isomerization of 13. The same adduct was obtained as the main product in the addition

of dichlorocarbene to 2-methylenenorbornane.

It proved impossible to secure a better elemental analysis of 18, owing to its tendency to lose a molecule of hydrogen chloride on heating.

1.1.2. Dehydrochlorination of exo-3,4-dichloro-2-methylbicyclo[3.2.1]oct-2-ene (18)

A solution of 18 (2.5 g; 13 mmoles) in dry pyridine (10ml) was stirred and heated at 110° for 2 h. After dilution with water, the solution was worked up in the usual way. The ether was distilled off and the product was fractionated through a Vigreux column to yield 3-chloro-2-methylenebicyclo[3.2.1]oct-3-ene (19) (1.05 g; 6.8 mmoles) 52%.

1.1.3. Addition of hydrogen chloride to 3-chloro-2-methylenebicyclo[3.2.1]oct-3-ene (19)

Dry hydrogen chloride was passed into a solution of 19 in carbon tetrachloride at -10°. After the disappearance of the diene, the NMR spectrum of the solution was examined. Three products were detected: 2,3-dichloro-2-methylbicyclo[3.2.1]oct-3-ene (20), exo-3,4-dichloro-2-methylbicyclo[3.2.1]oct-2-ene (18) and endo-3,4-dichloro-2-methylbicyclo[3.2.1]oct-2-ene (21) in the ratio 1:3:1 respectively. After three hours at room temperature the NMR spectrum indicated that 20 had converted completely to 18.

Passage of dry hydrogen chloride into a solution of 19 in chloroform at 45° gave only two compounds, namely 18 and 21 in the ratio 4:1.

1.1.4. Treatment of exo-3,4-dichloro-2-methylbicyclo[3.2.1]oct-2-ene (18) with aqueous silver nitrate.

To a solution of 18 (2.0 g; 10.6 mmoles) in 50% aqueous acetone (5 ml), a solution of silver nitrate (2.0 g) in water (3 ml) was added. The mixture was heated under reflux for 2 h. Silver chloride was separated by filtration and the filtrate was worked up in the usual fashion. The solvent was removed

and the remaining oil was distilled in vacuo. Two fractions were obtained. The first (41-42°/0.15 Torr; 0.79 g; 5.1 mmoles) 51% was identified as 3-chloro-2-methylenebicyclo[3.2.1]-oct-3-ene (19); the high boiling fraction (72-73°/0.15 Torr; 0.59 g; 3.4 mmoles) 34% proved to be 3-chloro-exo-4-hydroxy-2-methylbicyclo[3.2.1]oct-2-ene (23). This fraction crystallized on standing, and was further purified by sublimation: m.p. 66-67°.

3-chloro-exo-4-hydroxy-2-methylbicyclo[3.2.1]oct-2-ene (23). - M.p. 66-67°. IR. spectrum (in Nujol): max. at 3260(s), 1647(w), 1020(m) and 722(m) cm⁻¹ indicative of the hydroxy and chloro groups and an endocyclic, tetrasubstituted double bond.

C ₉ H ₁₃ ClO (172.70)	Calc. C 62.60	H 7.59	Cl 20.53%
	Found 62.61	7.59	20.65%

1.1.5. Hydrolysis of exo-3,4-dichloro-2-methylbicyclo[3.2.1]oct-2-ene (18)

exo-3,4-Dichloro-2-methylbicyclo[3.2.1]oct-2-ene (18) (0.5 g; 2.8 mmoles) in 65% aqueous acetone (23 ml) was stirred at room temperature for 3h. The solution was diluted with water and worked up the usual way to afford a mixture of 3-chloro-2-hydroxy-2-methylbicyclo[3.2.1]oct-3-ene (24) and 3-chloro-exo-4-hydroxy-2-methylbicyclo[3.2.1]oct-2-ene (23) in the ratio 1:3 (0.408 g; 2.35 mmoles) 85%. Separation was effected by GLC using a column (4.5 m, 8.0 mm) packed with 20% Carbowax 20M on Chromosorb W(80/100 mesh; acid washed and silanized), nitrogen as carrier gas (200 ml/min) and temperatures of 200° (injection) and 180° (column). The retention times were 30 min. for 23 and 25 min. for 24.

3-Chloro-2-hydroxy-2-methylbicyclo[3.2.1]oct-3-ene (24) was further purified by sublimation (50°/0.01 mm): m.p. 50-51°. IR. spectrum: max. at 3350(s), 3020(w), 1629(m), 842(w) and 740(s) cm⁻¹ characteristic of the hydroxy and chloro groups and an endocyclic, tetrasubstituted double bond. Mass spectrum: M⁺: 172.

1.1.6. NMR Data of Bicyclo[3.2.1]octene Derivatives

Compound	C(1)	C(4)	C(5)	C(2)subst.
<u>18</u>	2.49	4.17 $\underline{m}(J=2.8)$ ($^5J=1.3$)	2.69 $\underline{m}$	1.84 $\underline{d}(^5J=1.3)$
<u>19</u>	3.04 $\underline{d}$ of $\underline{m}$ ($J=4.5$)	6.21 $\underline{d}(^3J=7.3)$	2.65 $\underline{m}$	5.05 $\underline{s}$ and 4.82 $\underline{t}(J=1.2)$
<u>20</u>		6.09 $\underline{d}$ of $\underline{d}$ ($^3J=7.5$) ($^4J=1.3$)	2.70 $\underline{m}$	1.76 $\underline{s}$
<u>21</u>		4.95 $\underline{m}(^3J=4.9)$	2.65 $\underline{m}$	1.84 $\underline{s}$
<u>23</u>	2.44 $\underline{m}$	3.67 $\underline{m}(^3J=2.7)$ ($^5J=1.2$)	2.55 $\underline{m}$	1.81 $\underline{d}(^5J=1.2)$
<u>24</u>		6.00 $\underline{d}(^3J=7.3)$	2.60 $\underline{m}$	1.35 $\underline{s}$

1.2. Bicyclo[4.2.1]nonene derivatives

1.2.1. General procedure for the dichlorocarbene additions

The starting olefin (0.27 mole) in petroleum ether (250 ml) was stirred at 5° with sodium methoxide (60.0 g; 1.12 mole). Ethyl trichloroacetate (168.0 g; 0.88 mole) was then added dropwise over a period of 4 hours. The temperature was kept at 5-10° during the addition and subsequently at 10° for four more hours. Stirring was continued overnight while the mixture was allowed to reach room temperature. The brown mixture was poured onto ice and water and extracted with ether. The organic layer was separated, washed with water, a saturated NaCl solution, and dried over magnesium sulfate. Evaporation of ether and distillation in vacuo afforded the product.

Bicyclo[3.2.1]oct-2-ene (25), 3-chlorobicyclo[3.2.1]oct-2-ene (27) and exo-3,4-dichlorobicyclo[3.2.1]oct-2-ene (29) under the foregoing conditions gave in each case a single adduct, stable under the conditions of isolation and distillation (see table 6).

Table 6: CCl₂ adducts to 25, 27 and 29.

Olefin	Adduct	Boiling Point	Yield
<u>25</u>	<u>26</u>	77-78°/0.4 Torr	94%
<u>27</u>	<u>28</u>	83-84°/0.4 Torr	89%
<u>29</u>	<u>30</u>	102-103°/0.35 Torr	46%

exo-3,3-Dichlorotricyclo[4.2.1.0^{2,4}]nonane (26).- IR. spectrum: max. at 3010, 1035 and 1028 cm⁻¹ for the cyclopropane moiety. NMR. spectrum: 1.05 ppm (d of m, 1 H, ²J=12 Hz), 1.40-2.20 ppm (m, 10 H) and 2.55 ppm (m, 1 H). MS.: M⁺: 190, 192 and 194 in the ratio 9:6:1, characteristic of two chlorines.

C₉H₁₂Cl₂ (191.1) Calc. C 56.56 H 6.32 Cl 37.10%
Found 56.60 6.27 37.11%

exo-3,3,4-Trichlorotricyclo[4.2.1.0^{2,4}]nonane (28).- IR. spectrum: max. at 3000, 1063 and 1025 cm^{-1} for the cyclopropane moiety. NMR spectrum: 1.07 ppm (d of m, 1 H, $^2J=12$ Hz), 1.70-2.30 ppm (m, 7 H), 1.40-1.80 ppm (m, 3 H).

$\text{C}_9\text{H}_{11}\text{Cl}_3$ (225.5) Calc. C 48.00 H 4.90 Cl 47.20%

Found 47.87 4.93 47.21%

exo-3,3,4,5-Tetrachlorotricyclo[4.2.1.0^{2,4}]nonane (30).- IR. spectrum: max. at 3013, 1040 and 1005 cm^{-1} for the cyclopropane moiety. NMR spectrum: 1.15 ppm (d of m, 1 H, $^2J=12.2$ Hz), 1.50-2.90 ppm (m, 8 H), 4.88 ppm (fine t or d of d, 1 H, $^3J=1.8$ Hz). MS.: M^+ : four main peaks 258, 260, 262 and 264 in the ratio 27:36:18:4, characteristic of four chlorines.

$\text{C}_9\text{H}_{10}\text{Cl}_4$ (260.0) Calc. C 41.50 H 3.84 Cl 54.66%

Found 40.67 3.92 55.30

Double addition of dichlorocarbene to norbornene.

Norbornene (1) (9.5 g; 0.1 mole), chloroform (30 ml), benzyltriethylammonium chloride (0.4 g) and a 50% aqueous sodium hydroxide solution were stirred and heated at 45° for 24 h. After cooling, the mixture was diluted with water, the organic phase was separated and dried over calcium chloride. Evaporation of the solvent and distillation gave 29 (87%) and 30 (12%).

1.2.2. General procedure for the reductions of the tricyclic derivatives with lithium aluminium hydride (LAH)

The tricyclic compound (0.01 mole) in ether (or tetrahydrofuran) (5 ml) was added dropwise to a suspension of LAH (0.8 g; 0.021 mole) in ether (or THF) (15 ml) and the mixture was refluxed. The excess of LAH was then destroyed by careful addition of water, the aluminium and lithium hydroxides were filtered and the solution was dried over sodium sulfate. Evaporation of ether gave a crude mixture from which the products were isolated by GLC, using a 3 meter column packed with 5% SE-30 on Chromosorb G (acid washed and silanized), helium as

carrier gas (120 ml/min.), temperature 140-180° (table 7).

Table 7: LAH reductions of 26, 28 and 30

Reactant Solvent	Product ratio (%)			Anti/Syn Ratio	Overall Yield(%)	Reaction Time (h.)
	Anti	Syn	Parent			
<u>26</u> THF	<u>31</u> 58.5	<u>32</u> 29.2	<u>33</u> 12.2	2.0	82.5	27
<u>28</u> Et ₂ O	<u>34</u> 45.8	<u>35</u> 22.9	<u>36</u> 7.0	2.0	80.0	45
	<u>7</u> 13.3	<u>8</u> 8.6	<u>2 + 9</u> 2.4	1.6		
<u>30</u> Et ₂ O	<u>41</u> 44.0	<u>42</u> 7.0		5.7	90.0	80
	<u>43</u> 25.0	+ others 20.0				

exo-anti-3-Chlorotricyclo[4.2.1.0^{2,4}]nonane (31). IR. spectrum: max. at 3020, 1020 and 1010 cm⁻¹ (cyclopropane). MS.: M⁺: 156 and 158 in the ratio 3:1 (1 Cl).

exo-syn-3-Chlorotricyclo[4.2.1.0^{2,4}]nonane (32). IR. spectrum: max. at 3015, 1017 and 1010 cm⁻¹ (cyclopropane). MS.: M⁺: 156 and 158 in the ratio 3:1 (1 Cl).

exo-Tricyclo[4.2.1.0^{2,4}]nonane (33). IR. spectrum: max. at 3060, 3000, 1022, 1012 and 835 cm⁻¹ for the cyclopropane. MS.: M⁺: 122.

C₉H₁₄ (122.0) Calc. C 88.52 H 11.48%
Found 88.38 11.45%

exo-anti-3,4-Dichlorotricyclo[4.2.1.0^{2,4}]nonane (34). IR. spectrum: max. at 3038 and 1012 cm⁻¹ (cyclopropane). MS.: M⁺: 190, 192 and 194 in the ratio 9:6:1 (2 Cl).

exo-syn-3,4-Dichlorotricyclo[4.2.1.0^{2,4}]nonane (35). IR. spec-

trum: max. at 3045 and 1015 cm^{-1} (cyclopropane). MS.: M^+ : 190, 192 and 194 in the ratio 9:6:1 (2 Cl).

exo-4-Chlorotricyclo[4.2.1.0^{2,4}]nonane (36). - IR. spectrum: max. at 3070, 3000, 1035 and 1012 cm^{-1} (cyclopropane). NMR spectrum: 0.55-2.60 ppm (m). MS.: M^+ : 156 and 158 in the ratio 3:1 (1 Cl).

exo-anti-3,4,5-Trichlorotricyclo[4.2.1.0^{2,4}]nonane (41). - MS.: M^+ : 224, 226 and 228 in the ratio 3:3:1 (3Cl: the fourth peak was seen at high resolution).

exo-syn-3,4,5-Trichlorotricyclo[4.2.1.0^{2,4}]nonane (42). - MS.: M^+ : 224, 226 and 228 in the ratio 3:3:1 (3 Cl: the fourth peak was seen at high resolution).

Table 8: NMR data of the tricyclic derivatives

	X; Y; Z	Solvent	H_A	H_B
<u>31</u> anti	X=Cl Y=Z=H	CCl_4	2,75 ppm <u>t</u> ($^3\text{J}=3.0 \text{ Hz}$)	-
<u>32</u> syn	X=Cl Y=Z=H	CCl_4	3,77 ppm <u>t</u> ($^3\text{J}=8.0 \text{ Hz}$)	-
<u>34</u> anti	X=Y=Cl Z=H	CDCl_3	2,92 ppm <u>d</u> ($^3\text{J}=4.7 \text{ Hz}$)	-
<u>35</u> syn	X=Y=Cl Z=H	CDCl_3	3.65 ppm <u>d</u> ($^3\text{J}=9.3 \text{ Hz}$)	-
<u>41</u> anti	X=Y=Z=Cl	CCl_4	3.33 ppm <u>d</u> ($^3\text{J}=5.3 \text{ Hz}$)	4.62 ppm <u>m</u>
<u>42</u> syn	X=Y=Z=Cl	CCl_4	3.77 ppm <u>d</u> ($^3\text{J}=10.0 \text{ Hz}$)	4.75 ppm <u>m</u>
<u>43</u> anti	X=Z=Cl Y=H	CCl_4	3.19 ppm <u>t</u> ($^3\text{J}=3.5 \text{ Hz}$)	4.38 ppm <u>d</u> of <u>m</u> ($^3\text{J}=6.6 \text{ Hz}$)

exo-anti-3,5-Dichlorotricyclo[4.2.1.0^{2,4}]nonane (43). - IR. spectrum: max. at 3030, 1055 and 1015 cm^{-1} (cyclopropane). MS.: M^+ : 190, 192 and 194 in the ratio 9:6:1 (2 Cl).

Reductive dehalogenation with lithium aluminium deuteride

26 (1.0 g; 5.2 mmoles) in dry tetrahydrofurane (THF) (11 ml) was refluxed for 56 hours with lithium aluminium deuteride (LAD) (0.6 g; 14 mmoles). The resulting reaction mixture was diluted with pentane (50 ml) and filtered. LAD was washed with two portions of pentane (25 ml). The pentane fractions were stirred and two drops of D_2O were added to destroy the small amount of LAD still in solution. The solvent was then evaporated and the products were separated the usual way (vide supra). Analysis of the reaction mixture by GLC showed three compounds, 38, 40 and the deuterated analogue to 33 in the percentage ratio 18:74:8.

1.2.3. Cyclopropyl-allyl rearrangements

i/ Adduct 26 (30.0 g) was stirred and heated at 225-235° under nitrogen for two hours. After cooling, the black reaction mixture (26.0 g) was chromatographed rapidly over silica (300.0 g; 70-230 mesh ASTM), using light petroleum as eluant to give 3-chlorobicyclo[4.2.1]nona-2,4-diene (45) (2.0-4.0 g) (vide infra) and exo-2,3-dichlorobicyclo[4.2.1]non-3-ene (44) (14.0 g) in 47% yield.

exo-2,3-dichlorobicyclo[4.2.1]non-3-ene (44). - B.p. 107-109°/12 Torr. IR.: max. at 3030(w), 1643(m), 823(s) and 795(m) cm^{-1} for the C-H stretching, C=C and C-H out of plane deformations. NMR.: 1.30-2.90 ppm (m, 10 H), 4.53 ppm (d, 1 H, $^3\text{J}=4.7$ Hz), 5.96 ppm (d of d, 1 H, $^3\text{J}=5.3$ Hz).

$\text{C}_9\text{H}_{12}\text{Cl}_2$ (191.1)	Calc. C 56.55	H 6.27	Cl 37.20%
	Found 56.36	6.48	37.19%

ii/ Adduct 28 (18.0 g) was dissolved in decalin (100 ml) and heated under nitrogen at 180° for 18 hours. The solvent

was evaporated; an NMR spectrum of the residual oil revealed exo-2,3,4-trichlorobicyclo[4.2.1]non-3-ene (46) and 3,4,4-trichlorobicyclo[4.2.1]non-2-ene (47) in a ratio of 2:1. Distillation in vacuo of the mixture gave a sample of 47 suitable for NMR. and MS. analyses. On heating the reaction mixture for three more hours at 180°, 47 was entirely converted into 46. Total yield of product obtained by thermal rearrangement was 76%. exo-2,3,4-trichlorobicyclo[4.2.1]non-3-ene (46).- B.p. 93-95°/0.25 Torr. IR.: max. at 1603(s) for the dichlorinated double bond. NMR.: 1.10-2.70 ppm (m, 10 H), 4.96 ppm (d, 1 H, ³J=4.6 Hz). MS.: M⁺: 224, 226 and 228 in the ratio 3:3:1 (3 Cl).

C ₉ H ₁₁ Cl ₃	(225.5)	Calc.	C 47.81	H 4.90	Cl 47.29%
		Found	47.85	5.08	47.40%

The structure of 47 could not be unambiguously established, nevertheless the IR. spectrum revealed a characteristic strong band at 1590 cm⁻¹. Moreover, its NMR. spectrum and thermal conversion to 46 favour structure 47.

3,4,4-trichlorobicyclo[4.2.1]non-2-ene (47).- B.p. 93-94°/0.25 Torr. IR.: max. at 1590(s), 840(m) and 818(s) cm⁻¹. NMR.: 1.20-2.80 ppm (m, 9 H), 2.98 ppm (d of d, 1 H, ²J= -17.1 Hz, ³J=7.4 Hz), 5.08 ppm (d of d, 1 H, ³J=6.9 Hz, J=1.0 Hz). MS.: M⁺: 224, 226 and 228 in the ratio 3:3:1 (3 Cl).

iii/ Adduct 30 (5.5 g) was heated neat under nitrogen at 200° for 14 hours. On cooling, the black reaction mixture solidified. Recrystallization from light petroleum (b.p. 50-70°) and decolorization with activated charcoal afforded colorless crystals of exo-2,3,4,5-tetrachlorobicyclo[4.2.1]non-3-ene (48) (2.6 g) 47% yield.

exo-2,3,4,5-tetrachlorobicyclo[4.2.1]non-3-ene (48).- M.p. 92-95°. IR.: max. at 1615 cm⁻¹ characteristic of the tetrasubstituted double bond. NMR.: 1.40-3.05 ppm (m, 8 H), 4.72 ppm (d, 2 H, ³J=4.8 Hz).

C ₉ H ₁₀ Cl ₄	(260.0)	Calc.	C 41.50	H 3.85	Cl 54.50%
		Found	41.41	3.94	54.50%

1.2.4. Synthesis of bicyclo[4.2.1]nona-2,4-dienes

3-Chlorobicyclo[4.2.1]nona-2,4-diene (45). A solution of adduct 26 (45.0 g; 0.236 mole) in quinoline (150 ml) was stirred and heated at 200° under nitrogen for 4½ hours. After cooling, the black mixture was diluted with carbon tetrachloride and then washed several times with water, finally with 10% aqueous hydrochloric acid. The resulting organic layer was dried over CaCl₂. Evaporation of the solvent and distillation gave 45 (28.0 g; 0.181 mole) in 77% yield. IR.: max. at 3030(m), 1625(s), 805(w) and 719(w) cm⁻¹ for the diene system. UV.: λ_{max}. (in ethanol): 204 nm (ε = 2350), 223 nm (ε = 2470) and 265 nm (ε = 4300). NMR.: 1.25-2.08 ppm (m, 6 H), 2.33 ppm (m, 2 H), 5.72 ppm (d of d, 1 H, ³J=12 Hz, J=1.7 Hz), 6.08 ppm (d of d of m, 1 H, ³J=12 Hz, ³J=8.0 Hz), 6.22 ppm (d of m, 1 H, ³J=8.0 Hz). MS.: M⁺: 154 and 156 in the ratio 3:1 (1 Cl).

Bicyclo[4.2.1]non-3-ene (49). Diene 45 (6.0 g; 0.039 mole) in ethyl ether (40 ml) was added dropwise to a solution of sodium (10.0 g; 0.43 atg) in liquid ammonia (100 ml) over 1.5 h. Excess sodium was decomposed by addition of a 50% mixture of ether and methanol and the ammonia was allowed to evaporate. After dilution with water, the organic phase was washed several times with water, dried over Na₂SO₄ and distilled. Further distillation of the residue gave 49 (3.0 g; 0.0245 mole) in 63% yield. B.p. 168-169°/760 Torr. IR.: max. at 3010(m), 1660(m) and 1320(w) cm⁻¹ for the cis double bond. NMR.: 1.15-2.65 ppm (m, 12 H), 5.48 ppm (m, 2H). MS.: M⁺: 122.

C₉H₁₄ (122.0) Calc. C 88.52 H 11.48%

Found 88.46 11.48%

3,4-Dibromobicyclo[4.2.1]nonane (50). Bromine (2.6 g; 0.0162 mole) in carbon tetrachloride (2 ml) was added dropwise to a stirred mixture of 49 (2.0 g; 0.0162 mole) and ethanol (0.2 nl) in carbon tetrachloride (4 ml) at -5 to -1°. After addition, the mixture was allowed to reach room tempe-

perature and the solvent was evaporated. The crude solid was recrystallized from petroleum ether to give 50 (4.3 g; 0.053 mole) in 94% yield. M.p. 78-80°. NMR.: 1.45-3.05 ppm (m, 12 H), 4.41 ppm (m, 2 H). MS.: M^+ : 280, 282 and 284 in the ratio 1:2:1 (2 Br).

$C_9H_{14}Br_2$ (281.8)	Calc. C 38.29	H 4.97	Br 56.74%
	Found 38.43	5.00	56.55%

Bicyclo[4.2.1]nona-2,4-diene (51). Dibromo adduct 50 (5.0 g; 16.5 mmoles) in dimethylformamide (DMF) (15 ml) was added dropwise to a solution of potassium t-butoxide (6.0 g; 53.5 mmoles) in DMF (35 ml) under nitrogen at 0° during 40 minutes. The mixture was stirred for an additional hour and then allowed to reach room temperature. The solution was diluted with water and worked up the usual way to give 51 (1.2 g; 10.0 mmoles) in 60% yield and 3-bromobicyclo[4.2.1]non-3-ene (52) (0.9 g; 4.5 mmoles) in 30% yield.

Bicyclo[4.2.1]nona-2,4-diene (51).- B.p. 50°/12 Torr. IR.: max. at 3050(w), 3010(s), 1660(w), 1596(w) and 700(s) cm^{-1} characteristic of the diene. UV.: λ_{max} . (in ethanol): 204 nm ($\epsilon = 1500$) and 259 nm ($\epsilon = 5250$). NMR.: 1.60-2.25 ppm (m, 6 H), 2.66 ppm (m, 2 H), 5.65 ppm (m, 2 H) and 5.99 ppm (m, 2 H). MS.: M^+ : 120.
3-Bromobicyclo[4.2.1]non-3-ene (52).- B.p. 70°/0.1 Torr. The structure was elucidated by comparison with the chloro analogue 58(vide infra). NMR.: 1.15-2.90 ppm (m, 12 H) and 6.08 ppm (broad d of d, 1 H).

3,4-Dichlorobicyclo[4.2.1]nona-2,4-diene (53). Tetrachloro compound 44 (1.4 g; 5.4 mmoles) in acetone (40 ml) and zinc dust (1.5 g) was heated under reflux for 3 hours. The mixture was filtered and the solvent was distilled off. The residue was dissolved in ethyl ether, washed with water and with 10% hydrochloric acid and finally dried over Na_2SO_4 . Evaporation of ether gave 53 (1.0 g; 5.3 mmoles) in 98% yield. IR.: max. at 3030(m), 1603(m), 1587(w), 819(w), 808(w) and 713(w) cm^{-1} typical of a diene. NMR.: 1.70-2.25 ppm (m, 6 H), 2.75 ppm (m, 2H)

and 6.47 ppm (d, 2 H, $^3J=8.7$ Hz). UV.: λ_{max} . (in ethanol): 206 nm ($\epsilon = 6150$), 223 nm ($\epsilon = 5160$) and 271 nm ($\epsilon = 7400$). MS.: M^+ : 188, 190 and 192 in the ratio 9:6:1 (2 Cl).

2. PHOTOCHEMICAL ISOMERIZATIONS

2.1. Direct irradiations

Solutions of 51, 45 and 53 (1.67, 1.30 and 0.53 mmoles respectively) in n-hexane (10 ml) under nitrogen were stirred and irradiated in quartz tubes with an unfiltered 200-W Hano-via lamp at 25°. Periodically, samples were extracted and monitored by vapor-phase chromatography (5% SE-30 on Chromosorb G, column temperature of 100° for the products from compound 51, and 25% Apiezon L on Chromosorb W, column temperature of 120° for the products from compounds 45 and 53). In all cases, the exo isomer had the shorter retention time. Products from dienes 51 and 45 were separated by GLC, using the conditions described for the analytical work, and their structures were determined by NMR. spectroscopy:

exo-Tricyclo[4.2.1.0^{2,5}]non-3-ene (54).- 0.92 ppm and 1.50 ppm (m, 6 H), 1.88 ppm (m, 2 H), 2.36 ppm (s, 2 H) and 5.82 ppm (s, 2 H).

endo-Tricyclo[4.2.1.0^{2,5}]non-3-ene (55).- 1.34 ppm (m, 4 H), 1.56 ppm (m, 2 H), 2.22 ppm (m, 2 H), 2.90 ppm (d of m, 2 H, $^3J=4.5$ Hz) and 6.28 ppm (s, 2 H).

exo-3-Chlorotricyclo[4.2.1.0^{2,5}]non-3-ene (56).- 0.86-1.80 ppm (m, 6 H), 2.08 ppm (m, 2 H), 2.49 ppm (d of m, 1 H, $^3J=3.3$ Hz), 2.70 ppm (d of m, 1 H, $^3J=3.3$ Hz) and 5.70 ppm (s, 1 H).

endo-3-Chlorotricyclo[4.2.1.0^{2,5}]non-3-ene (67).- 1.44 ppm (m, 4 H), 1.63 ppm (m, 2 H), 2.28 ppm (m, 2 H), 2.84 ppm (d of d, 1 H, $^3J=5.2$ Hz, $^3J=5.1$ Hz), 3.16 ppm (d of d, 1 H, $^3J=5.2$ Hz, $^3J=5.0$ Hz) and 6.07 ppm (s, 1 H).

exo- and endo-3,4-Dichlorotricyclo[4.2.1.0^{2,5}]non-3-ene (58 and 59) proved impossible to separate. Their structures were

determined on the basis of their retention times in GLC., assuming that the exo derivative has the shorter retention time.

2.2. Sensitized irradiations

The procedure described above was used, but taking now pyrex tubes ($h\nu > 300$ nm) and adding one molar acetophenone for compounds 51 and 45, and taking acetone as solvent and sensitizer for compound 53.

3. REDUCTIVE DEHALOGENATIONS OF BICYCLIC HALIDES

3.1. Lithium aluminium hydride

3.1.1. Reduction of exo-3,4-dichloro-2-methylbicyclo[3.2.1]oct-2-ene (18)

A solution of 18 (4.0 g; 21 mmoles) in anhydrous ether (10 ml) was added dropwise to a suspension of LAH (1.5 g; 39 mmoles) in anhydrous ether (35 ml). The mixture was stirred and heated under reflux for 18 hours. The excess of reagent was destroyed by dropwise addition of a small quantity of water. The resulting solution was filtered and dried over magnesium sulfate. The ether was removed and the product was distilled under reduced pressure (53-54°/0.45 Torr; 3.0 g; 19.1 mmoles) 91%. IR. revealed the presence of two compounds ($C=C$: 1667 and 1632 cm^{-1}). Separation was effected by GLC., using a column (4.5 m/8.0 mm) packed with 20% Apiezon L on Chromosorb W(80/100 mesh, acid washed and silanized), nitrogen as carrier gas (120 ml/min.) and temperatures of 170° (injection) and 135° (column).

The major component (4:1) had the longer retention time (30.5 min.) and was 3-chloro-endo-2-methylbicyclo[3.2.1]oct-3-ene (63).- IR. spectrum: max. at 3040(w), 1632(s), 842(s) and 679(s) characteristic of the trisubstituted double bond and the C-Cl bond. NMR.: 1.10 ppm (d, 3 H, $^3J=7.2$ Hz), 1.50-2.90 ppm (m, 9 H) and 5.91 ppm (d of d, 1 H, $^3J=6.7$ Hz, $^4J=2.0$ Hz).

$C_9H_{13}Cl$ (156.65)	Calc. C 69.01	H 8.37	Cl 22.66%
	Found 69.05	8.61	22.44%

The minor component (retention time of 26.5 min.) was 3-chloro-2-methylbicyclo[3.2.1]oct-2-ene (64).- IR. spectrum: max. at 1667(w) and 720(m) cm^{-1} due to the tetrasubstituted double bond and C-Cl bond. NMR.: 1.40 ppm-2.65 ppm (m), 1.78 ppm (d, $^5J=1.7$ Hz).

$C_9H_{13}Cl$ (156.65)	Calc. C 69.01	H 8.37	Cl 22.66%
	Found 69.10	8.50	22.51%

Both compounds were stable under the separation conditions.

Reduction of the mixture of 18 and 21 with LAH

The reaction was carried out in exactly the same way as for pure 18 (see above). From the mixture of 18 and 21 (4:1; 3.5 g; 18.4 mmols), 63 and 64 were obtained in a ratio 7:3 (2.38 g; 15.2 mmols) 84% yield.

3.1.2. Reduction of exo-3,4-dichloro-2-phenylbicyclo[3.2.1]oct-2-ene (62)

Compound 62 (2.53 g; 0.01 mole) in dry ethyl ether (5 ml) was added dropwise to a suspension of LAH (0.8 g) in dry ethyl ether (20 ml). The mixture was then stirred and heated under reflux for 18 hours. Excess LAH was decomposed by careful addition of water and the ethereal solution was dried over anhydrous sodium sulfate. Subsequent evaporation of the ether gave 65 and 66 (1.6 g; 7.7 mmols) 73% in the ratio of 45:55, as determined by both NMR. and GLC. Separation of the two isomers was effected by preparative GLC., using a column (4.5 m/8.0 mm) packed with 20% Apiezon L on Chromosorb W (80/100 mesh; acid washed and silanized), nitrogen as carrier gas (80 ml/min) and temperatures of 240° (injection) and 215° (column). The retention times were 68 min. for 66 and 73 min. for 65.

3-Chloro-endo-2-phenylbicyclo[3.2.1]oct-3-ene (65).- UV. spectrum: λ_{max} . (in hexane) 214 nm ($\epsilon = 12200$). MS.: M^+ : 218.

NMR.: 1.70 ppm (m, 6 H), 2.52 ppm (m, 2 H), 4.03 ppm (d of m,

1 H, $^3J=4.6$ Hz), 6.31 ppm (d of d, $^3J=6.7$ Hz, $^4J=1.5$ Hz) and 7.27 ppm (m, 5 H).

3-Chloro-2-phenylbicyclo[3.2.1]oct-2-ene (66). - NMR. spectrum:

7.33 ppm (m, 5 H), 1.40-2.90 ppm (m, 10 H). UV. spectrum:

λ_{max} . (in hexane) 212 nm ($\epsilon = 7800$) and 245 nm ($\epsilon = 6550$). MS.: M^+ : 218.

3.1.3. 3-Chlorobicyclo[4.2.1]non-2-ene (67). 44 (11.0 g; 0.058 mole) in ethyl ether (20 ml) was added dropwise to a suspension of lithium aluminium hydride (4.5 g; 0.12 mole) in ethyl ether (90 ml); the mixture was heated under reflux for 48 h. Excess of LAH was decomposed by careful addition of water; the ethereal layer was removed and dried over MgSO_4 . The solvent was evaporated and distillation of the residue in vacuo gave 67 (6.9 g; 0.044 mole) in 76% yield. B.p. $82-83^\circ/11$ Torr. IR.: max. at 3039(w), 1643(s), 839(m) and 820(s) cm^{-1} . NMR.: 1.40-2.90 ppm (m, 12 H), 6.18 ppm (d of d, 1 H, $^3J=9.3$ Hz, $^4J=1.5$ Hz). MS.: M^+ : 156 and 158 in the ratio 3:1 (1 Cl).

$\text{C}_9\text{H}_{16}\text{Cl}$ (175.72)	Calc. C 69.02	H 8.37	Cl 22.60%
	Found 69.01	8.53	22.57%

3.2. Tri-n-butyltin hydride and sodium borohydride

3.2.1. Reduction of exo-3,4-dichloro-2-methylbicyclo[3.2.1]-oct-2-ene (18) with TBTH

A mixture of 18 (5.0 g; 26 mmoles) and tri-n-butyltin hydride (TBTH) (9.0 g; 31 mmoles) was stirred and heated at 80° for 18 hours under nitrogen. After dilution with anhydrous ether (100 ml), ammonia was passed through the mixture until precipitation of the white quaternary ammonium salt of TBT-chloride was complete. After filtration and evaporation of the solvent, the residual oil was purified by column chromatography (basic alumina, Merck activity grade I, petroleum ether as eluant) followed by distillation in vacuo to yield a mixture (56%) of 63 and 64 in the ratio 1:4.

3.2.2. Treatment of exo-3,4-dichloro-2-phenylbicyclo[3.2.1]-oct-2-ene (62) with TBTH

a) Compound 62 (2.53 g; 0.01 mole) was stirred and heated with TBTH (3.5 g; 12 mmoles) without solvent at 80° under nitrogen for 20 hours. Column chromatography (basic alumina, Merck activity grade I, using petroleum ether as eluant) of the resulting reaction mixture gave 65 and 66 (1.7 g; 8.2 mmoles) 82% yield in the ratio 1:6.

b) Compound 62 (1.0 g; 4.0 mmoles) and TBTH (1.4 g; 5.1 mmoles) were dissolved in ether (10 ml) and the mixture was refluxed under nitrogen for 18 hours. After evaporation of the ether, the mixture was chromatographed over basic alumina (see above) to give 65 and 66 (0.6 g; 2.7 mmoles) 69% yield in the ratio 1:6.

Compounds 65 and 66 were stable under the conditions used for both the LAH and TBTH reductions.

3.2.3. 3-Chlorobicyclo[4.2.1]non-3-ene (68)

44 (3.0 g; 15.7 mmoles) and tri-n-butyltin hydride (5.0 g 17.2 mmoles) were dissolved in ethyl ether (30 ml) and heated under reflux for 20 hours under nitrogen. Ether and tri-n-butyltin chloride were removed by distillation. The residue was chromatographed over neutral alumina (60.0 g) to give a mixture of 67 and 68 (1.5 g; 9.6 mmoles) in a ratio of 1:4 in a 61% yield. A sample of pure 68 was isolated for mass spectral analysis. NMR.: 1.35-2.80 ppm (m, 12 H), 5.78 ppm (d of d of m, 1 H). MS.: M⁺: 156 and 158 in the ratio 3:1 (1 Cl).

3.2.4. Reduction of exo-3,4-dichloro-2-methylbicyclo[3.2.1]-oct-2-ene (18) with sodium borohydride.

To a stirred solution of sodium borohydride (3.4 g; 90 mmoles) in 80% aqueous diglyme (50 ml) 18 (2.0 g; 13.5 mmoles) was added. The mixture was then heated at 50° for 24 hours under nitrogen. After cooling and dilution with water, the mixture was worked up and the residual oil was purified by column

chromatography (silica gel Merck, 70/325 mesh) to yield a mixture (1.33 g) of 3-chloro-endo-2-methylbicyclo[3.2.1]oct-3-ene (63), 3-chloro-2-methylbicyclo[3.2.1]oct-2-ene (64), 3-chloro-2-hydroxy-2-methylbicyclo[3.2.1]oct-3-ene (24), 3-chloro-exo-4-hydroxy-2-methylbicyclo[3.2.1]oct-2-ene (23) and 3-chloro-2-methylenebicyclo[3.2.1]oct-3-ene (19) in a percentage ratio of 28, 14, 16, 32 and 10, respectively.

3.3. Dissolving metal reductions

3.3.1. General procedure for the reductive dehalogenations

The starting chloro compound (8.4 mmoles) in dry ethyl ether (20 ml) was added dropwise to a solution of sodium (6.0 g; 0.26 atg) in liquid ammonia (100 ml), condensed in a dry ice-aceton bath, over a period of one hour. The mixture was then stirred for another hour and ammonia was allowed to evaporate. At the same time, a 50% mixture of methanol in ether was added dropwise to destroy the large excess of sodium. The white suspension was diluted with water, the organic phase separated and the aqueous phase extracted three times with ether. The combined ethereal fractions were then washed several times with water and finally with a saturated sodium chloride solution and dried over sodium sulfate. Ether was distilled off to yield the crude product.

Reactant	Product	Yield (%)	m.p. or b.p.	Means of purification
<u>44</u>	<u>49</u>	68	168-169°/760mm	Distillation
<u>46</u>	<u>69</u>	55	57-61°	Sublimation
<u>48</u>	<u>49</u>	31	168-169°/760mm	Distillation

endo-Tricyclo[4.2.1.0^{2,4}]nonane (69).- IR. spectrum: max. at 3070(m), 3000(m), 1028(w), 1018(w) and 836(w) cm⁻¹ for the

cyclopropane moiety. NMR.: 0.00-0.70 ppm (m, 2 H) and 0.75-2.70 ppm (m, 10 H). MS.: M^+ : 122.

C_9H_{14} (122.0) Calc. C 88.52 H 11.48%
Found 88.49 11.56%

The endo configuration was elucidated from the fact that 69 was different to its known exo isomer 33. Compound 69 (and 33) both displayed nine ^{13}C chemical shifts having values of 36.334, 32.955, 32.607, 32.409, 30.175, 29.082, 19.799, 9.684 and 4.360 ppm (and 34.452, 33.608, 32.367, 32.168, 31.523, 29.140, 19.112, 10.822 and 5.109 ppm) respectively with respect to tetramethylsilane taken as 0.000 ppm.

3.3.2. Synthesis of 2,3,4-trichlorobicyclo[3.2.1]oct-2-ene (80)

2,2-Dichlorobicyclo[2.2.1]heptane (77): Norcamphor (5.0 g; 45.5 mmoles) in benzene (3 ml) was added dropwise to a suspension of phosphorous pentachloride (9.4 g; 45.5 mmoles) in benzene (5 ml) at 10-20° over a period of 20 minutes. The mixture was then allowed to reach room temperature and was stirred for a further hour. Evaporation of benzene and phosphorous oxychloride gave a crude material, which was distilled under reduced pressure to give 77 (5.7 g; 34.5 mmoles) in 76% yield. B.p. 64-65°/11 Torr.

2-Chlorobicyclo[2.2.1]hept-2-ene (78): 77 (2.0 g; 12.1 mmoles) in dimethylformamide (DMF) (10 ml) was added to a solution of potassium t-butoxide (3.5 g) in DMF (20 ml) under nitrogen at 0° over a period of 15 minutes. The mixture was then stirred for one hour at 0° and was allowed to reach room temperature. After dilution with water, the organic phase was worked up the usual way to remove DMF. After having distilled off ether, the crude material was fractionated to give 78 (1.2 g; 9.35 mmoles) in 77% yield. B.p. 144-146°/760 Torr. NMR: 1.00-1.90 ppm (m, 6 H), 2.93 ppm (m, 2 H) and 5.84 ppm (d of m, 1 H, $^3J=3.4$ Hz).

Dichlorocarbene addition to 2-chlorobicyclo[2.2.1]hept-2-ene

Sodium methoxide (2.5 g; 46.0 mmoles) was added to a solution of 78 (1.6 g; 12.5 mmoles) in petroleum ether (10 ml) and the mixture was cooled at 5-10° for the dropwise addition of ethyl trichloroacetate (7.8 g; 41.0 mmoles). After the addition (30 minutes), the mixture was kept at the same temperature and then allowed to reach room temperature. After having been stirred overnight, the dark brown mixture was poured onto ice and worked up. Ether was then evaporated and the residue was distilled in vacuo to give a mixture of the two isomers 79 and 80 (1.8 g; 8.6 mmoles) 68% in the ratio 1:2. B.p. 74-76°/0.1 Torr. Stirring and heating of this mixture neat at 160° under nitrogen for 90 minutes resulted in the complete isomerization of 79 into 80, and also into about 10% of the endo isomer 81. MS.: M⁺: 210, 212 and 214 in the ratio 3:3:1 (3 Cl).

exo-2,3,4-Trichlorobicyclo[3.2.1]oct-2-ene (80).- NMR.: 1.30-3.05 ppm (m, 8 H) and 4.34 ppm (d, 1 H, ³J=2.7 Hz).

3,4,4-Trichlorobicyclo[3.2.1]oct-2-ene (79).- NMR.: 1.30-3.35 ppm (m, 8 H) and 6.18 ppm (d of d, 1 H, ³J=7.5 Hz, J=1.4 Hz).

endo-2,3,4-Trichlorobicyclo[3.2.1]oct-2-ene (81).- detected in the mixture by its exo allylic proton in NMR.: 5.02 ppm (d, 1 H, ³J=4.4 Hz).

3.3.3. Synthesis of exo- and endo-2,3,4-trichlorobicyclo[5.2.1]-dec-3-enes (85 + 86)

Dichlorocarbene addition to 3-chlorobicyclo[4.2.1]non-2-ene (67)

The method described above was used starting from 67 (5.0 g; 32.0 mmoles) and sodium methoxide (7.2 g; 133 mmoles) in petroleum ether (30 ml) and adding ethyl trichloroacetate (20.0 g; 105.0 mmoles). After usual work up, distillation in vacuo gave a mixture of 83 and 84 (5.8 g; 25.0 mmoles) 76% in the ratio 86:14. B.p. 85-87°/0.08 Torr.

exo- and endo-3,3,4-Trichlorotricyclo[5.2.1.0^{2,4}]decanes (83 and 84) proved impossible to separate, as the temperature required on GLC led to decomposition. NMR.: 1.00-2.90 ppm (m). IR spectrum: max. at 3062(w) and 1023(m) cm^{-1} (cyclopropane). MS.: M^+ : 238, 240 and 242 in the ratio 3:3:1 (3 Cl).

exo- and endo-2,3,4-Trichlorobicyclo[5.2.1]dec-3-ene (85 + 86)

A mixture of 83 and 84 in the ratio 86:14 (1.5 g) was stirred and heated under nitrogen at 220° for one and a half hour. After cooling, the dark residue was distilled in vacuo to yield a mixture of the two isomers 85 and 86 (1.2 g) 80% in the ratio 54:46. B.p. 90°/0.1 Torr. IR. spectrum: max. at 1602(s) and 1598(s) for the tetrasubstituted double bonds.

Separation was effected by GLC on a F21 Perkin-Elmer instrument, using a column (3.0 m/8.0 mm) packed with 20% FFAP on Chromosorb W (80/100 mesh; acid washed and silanized), nitrogen as carrier gas (140 ml/min) and temperatures of 200° (injection) and 170° (column).

exo-2,3,4-Trichlorobicyclo[5.2.1]dec-3-ene (85).- NMR.: 1.18-2.90 ppm (m, 12 H) and 5.24 ppm (d, 1 H, $^3\text{J}=7.0$ Hz). MS.: M^+ : 238, 240 and 242 in the ratio 3:3:1 (3 Cl).

endo-2,3,4-Trichlorobicyclo[5.2.1]dec-3-ene (86).- NMR.: 1.10-2.72 ppm (m, 12 H) and 5.25 ppm (d, 1 H, $^3\text{J}=3.9$ Hz). MS.: M^+ : 238, 240 and 242 in the ratio 3:3:1 (3 Cl).

3.3.4. Synthesis of 1,2,3-trichlorocycloheptene (94)

1-Chlorocyclohexene (92): Cyclohexanone (91) (10.0 g; 0.102 mole) was added dropwise to phosphorous pentachloride (21.0 g; 0.1 mole) at a temperature of 10-20°. The mixture was then allowed to reach room temperature and phosphorous oxichloride was evaporated. The yellowish residue was dissolved in dimethylformamide (DMF) (30 ml) and was added slowly to a solution of potassium t-butoxide (18.0 g) in DMF (60 ml) at 0° under nitrogen. After having reached room temperature, the mixture was worked up the usual way and the residue was distilled

to give 92 (10.0 g; 0.086 mole) in 84% yield. B.p. 139-141°/760 Torr. NMR.: 1.35-2.15 ppm (m, 8 H) and 5.30 ppm (m, 1 H).

1,2,2-Trichlorobicyclo[4.1.0^{1,3}]heptane (93): The usual procedure for the generation of dichlorocarbene was used starting from 92 (9.5 g; 0.081 mole), sodium methoxide (20.0 g; 0.370 mole), petroleum ether (80 ml) and ethyl trichloroacetate (56.0 g; 0.293 mole). Work up and distillation in vacuo yielded 93 (15.0 g; 0.075 mole) 92%. B.p. 59°/0.25 Torr. IR. spectrum: max. at 3018(w) cm⁻¹ for the cyclopropane. NMR.: 1.20-2.50 ppm (m). MS.: M⁺-Cl: 163, 165 and 167 in the ratio 9:6:1 (2 Cl).

1,2,3-Trichlorocycloheptene (94): 93 (3.0 g; 0.015 mole) was stirred and heated at 200° under nitrogen for 2 hours and 15 min. After cooling, the black reaction mixture was chromatographed over silica gel (Merck, 70-230 mesh), using petroleum ether as eluant and taking fractions of 25 ml. Two compounds were isolated: diene 95 (c.a. 1.5 g) and the trichlorinated cycloheptene 94 (1.23 g; 6.2 mmoles) 41%.

1,2-Dichlorocyclohepta-1,3-diene (95).- NMR.: 1.50-2.60 ppm (m, 6 H), 5.92 ppm (d of d of d, 1 H, ³J=10 Hz, ³J=3.3-4.0 Hz) and 6.43 ppm (d of d of d, 1 H, ³J=10.0 Hz and ⁴J=1.4 Hz).

1,2,3-Trichlorocycloheptene (94).- B.p. 58-60°/0.25 Torr. NMR.: 1.25-3.05 ppm (m, 8 H) and 5.30 ppm (m, 1 H). MS.: M⁺: 198, 200 and 202 in the ratio 3:3:1 (3 Cl).

3.3.5. Reductive dechlorinations of the mono- and bicyclic trichloro compounds

The general procedure described in section 3.3.1. has been used. The products were isolated and purified by vapor phase chromatography on a model 990 Perkin-Elmer instrument, using columns (10'x3/8") packed with 20% Carbowax 20M or 20% FFAP on Chromosorb W (80/100 mesh; acid washed and silanized) and helium as carrier gas (120-140 ml/min.).

Starting material (ratios)	Products (ratios)	Yields (%)	Columns	Temperatures
<u>80</u> + <u>81</u> (90 : 10)	<u>25</u>	40 ^{b)}	--	--
<u>83</u> + <u>84</u> (86 : 14)	<u>87</u> + <u>88</u> ^{a)} (64 : 36)	40 ^{c)}	Carbowax 20M	140°
<u>85</u> + <u>86</u> (54 : 46)	<u>87</u> + <u>88</u> ^{a)} (89 : 11)	35 ^{c)}	Carbowax 20M	140°
<u>93</u>	<u>96</u>	-- ^{d)}	FFAP	90°
<u>94</u>	<u>96</u> + <u>97</u> (55 : 45)	30	FFAP	90°

a) These mixtures were purified without isolating each isomer

b) Yield estimated from the NMR. spectrum of the crude product

c) Yield determined after purification by GLC.

d) Reaction carried out on a small scale to get 96 as a reference.

exo- and endo-Tricyclo[5.2.1.0^{2,4}]decane (87 and 88):- IR. spectrum: max. at 3062(w) and 1023(m) cm^{-1} for the cyclopropane. NMR.: 0.00-2.75 ppm (broad and complex m). MS.: M^+ : 136.

Bicyclo[4.2.1]non-2-ene (89): 67 (1.5 g; 9.0 mmoles) was treated with sodium in liquid ammonia (see section 3.3.1.) and gave quite pure 89 (0.87 g; 7.2 mmoles) in 79% yield. IR. spectrum: max. at 3010(s) and 1645(m) cm^{-1} for the cis double bond. NMR.: 1.25-2.90 ppm (m, 12 H), 5.35-6.30 ppm (m, 2 H). MS.: M^+ : 122.

Addition of methylene to bicyclo[4.2.1]non-2-ene (89): Zinc-Copper couple (1.5 g), prepared according to Shank and Shechter [226], was added to a mixture of methylene bromide (3.5 g) iodine (100 mg) and ethyl ether (12 ml). The mixture was refluxed for half an hour and 89 (0.5 g; 4.1 mmoles) in ethyl ether (2 ml) was added dropwise. The mixture was then refluxed for a further 55 hours, cooled and filtered through celite.

The ethereal solution was washed with 5% hydrochloric acid, sodium bicarbonate and saturated sodium chloride and dried over sodium sulfate. The solvent was then distilled off and the residue was purified by vapor phase chromatography, using a column packed with 20% Carbowax 20M on Chromosorb W (see above the general procedure for the reductive dehalogenations). At 140°, a mixture of 87 and 88 (160 mg; 1.23 mmole) 30% in the ratio 83:17 was separated from unreacted starting material.

Reductive dechlorination of 3,4-dichlorobicyclo[4.2.1]nona-2,4-diene (53)

Compound 53 (1.0 g; 5.3 mmoles) in ethyl ether (12 ml) was added to a solution of sodium (3.3 g; 0.14 atg) in liquid ammonia (40 ml) over a period of 30 minutes. Work up the usual way gave 49 (0.38 g; 3.2 mmoles) 60%.

3.3.6. Hydrogenolysis of the cyclopropane derivatives (33+69)

A mixture of 33 (or 69) (1.0 g), a catalytic amount of platinum oxide and acetic acid (20 ml) was placed in the Parr apparatus. A hydrogen pressure of 3 atmospheres was set up and the flask was shaken at 60-70° for 4 hours. After cooling, the mixture was worked up the usual fashion and distillation of ether gave a residual oil (c.a. 0.8 g), which was submitted to analytical GLC. A mixture of two compounds in the percentage ratio 52:48 (or 27:73) was detected. Separation of this mixture by preparative GLC. on a 990 Perkin-Elmer instrument, using a column (10'x3/8") packed with 20% FFAP on Chromosorb W (80/100 mesh; acid washed and silanized), helium as carrier gas (120 ml/min.) and temperatures of 180° (injection) and 80° (column), gave:

3-Methylbicyclo[3.2.1]octane (98). - NMR.: 0.82 ppm (d, 3 H, ³J=5.5 Hz), 0.95-1.85 ppm (m, 9 H) and 2.15 ppm (broad m, 2 H). MS.: M⁺: 124.

Bicyclo[4.2.1]nonane (99). - NMR.: 0.85-2.25 ppm (m). MS.: M⁺: 124.

4. SYNTHESIS OF BICYCLO[4.2.1]NONAN-3-ONE (112)

i) 3-Chlorobicyclo[4.2.1]non-2-ene (67) (6.0 g; 38.3 mmol) was stirred at 0° with conc. sulfuric acid (20 ml) for 11 hours. After dilution with water, the mixture was extracted with ether and worked up the usual way. Distillation of the solvent and sublimation of the residue gave the ketone 112 (1.45 g; 10.6 mmol) in 28% yield.

ii) Hydroboration: freshly distilled boron trifluoride etherate (3.9 g; 0.27 mole) was added to a stirred solution of bicyclo[4.2.1]non-3-ene (49) (5.0 g; 0.041 mole) and sodium borohydride (0.76 g) in diglyme (20 ml) under oxygen-free nitrogen over 20 min., while the temperature was maintained at 20-25°. The mixture was stirred for an extra hour, and the water was slowly added to decompose excess hydride. The resultant organoboronic acid was oxidized at 30-50° by adding 3N sodium hydroxide and 30% aqueous hydrogen peroxide. The reaction mixture was stirred for one hour at room temperature and extracted with ether and worked up as usual. Distillation of the solvent and chromatography of the residue over silica (50% ether in petroleum ether as eluant) afforded bicyclo[4.2.1]nonan-3-ol (115) (4.0 g; 0.027 mole) in 70% yield. Analytical GLC. (9% FFAP on Chromosorb W, 80/100 mesh, acid washed and silanized, 3m x 2mm, 120°) showed one compound in at least 95% purity. The configuration of the C3 hydroxyl group is most probably exo. IR. spectrum: max. at 3325(s) cm^{-1} for the hydroxy group. NMR.: 1.05-2.58 ppm (m, 14 H), 2.81 ppm (s, 1 H, exchangeable by deuterium), 3.70 ppm (broad m, 1 H). MS.: M^+ : 140.

$\text{C}_9\text{H}_{16}\text{O}$ (140.0)	Calc. C 77.14	H 11.42	O 11.42%
	Found 77.22	11.39	11.44%

iii) Oxidation: a solution of $\text{Na}_2\text{Cr}_2\text{O}_7 \cdot 2\text{H}_2\text{O}$ (0.72 g), conc. sulfuric acid (0.6 ml) and water (3 ml) was added dropwise over 15 min. to a solution of 115 (0.9 g; 6.43 mmol) in ether (4 ml). The mixture was stirred at room temperature for

4 hours, poured onto ice and worked up. Excess ether was evaporated, bicyclo[4.2.1]nonan-3-one (112) was obtained as a colourless solid (0.72 g; 5.22 mmoles) in 81% yield. Its purity was checked by GLC. (9% FFAP on Chromosorb W, acid washed and silanized, 3m x 2mm column, 120°) and found to be >99%. M.p. 118-120°. IR. spectrum: max at 1705 cm⁻¹. MS.: M⁺: 138.

C ₉ H ₁₄ O (138.0)	Calc. C	78.40	H	10.17	O	11.45%
	Found	78.31		10.72		10.97%

* * *

SUMMARY

It has been shown in the present work that the use of dichlorocarbene for ring enlargements is of great synthetic value, when the cyclopropane adducts can readily undergo ring opening. Thus, the dichlorocarbene adducts to norbornene rearrange at room temperature to give the bicyclo[3.2.1]octene system. However, dichlorocarbene adducts to bicyclo[3.2.1]oct-2-ene and its mono- and dichloro derivatives exhibit a remarkable stability up to 180°, or even 220° in some cases.

The thermal stability of these compounds made them suitable for the study of the reductive dehalogenation of cyclopropyl and bridgehead halides by means of lithium aluminium hydride. It has been demonstrated that such reductions do not undergo an S_N2 mechanism, as it was previously thought, but rather a direct attack of the hydride on chlorine takes place. The resulting carbanion could be responsible for the retention of configuration, which has been observed in the reduction of fluorochloro derivatives. Moreover, investigation of the reduction of di-, tri- and tetrachloro tricyclic compounds showed an increasing reactivity in going from alkyl to bridgehead to cyclopropyl halides.

Thermal cyclopropyl-allyl transpositions of the dichlorocarbene adducts can be accompanied by some elimination of hydrogen chloride. Thus, depending on the conditions, bicyclo[4.2.1]nonenyl and/or bicyclo[4.2.1]nonadienyl chlorides were

obtained in variable yields.

Direct or triplet sensitized irradiations of bicyclo-[4.2.1]nona-2,4-diene and its mono- and dichloro derivatives give cyclobutene compounds. These electrocyclic ring closures occur in a disrotatory mode. The presence of one, and then two chlorines in the conjugated system was found to affect considerably the course of the photochemical reactions. Thus, the product distribution arising from direct irradiation of 3,4-dichlorobicyclo[4.2.1]nona-2,4-diene is very similar to that found in the photosensitized experiment. These results are interpreted in terms of an intramolecular heavy atom effect due to the halogens directly affixed to the chromophore.

Very often, the use of thermally rearranged products in synthesis requires either the substitution of chlorines by other functional groups, or simply their elimination. Treatment of allylic halides with LiAlH_4 , Bu_3SnH or NaBH_4 results in a complete dehalogenation. However, the use of metal hydrides in these reductions engenders very often a migration of the double bond. Further investigation of the reductions with lithium aluminium hydride (LAH) showed that the entrance of the hydride and the departure of the halogen take place in a synfacial manner. No trace of product arising from a simple bimolecular displacement, $\text{S}_{\text{N}}2$, has been detected. These results indicate that the metal hydride is operating directly on an ion pair in either an $\text{S}_{\text{N}}2'$ or $\text{S}_{\text{N}}\text{i}'$ process.

Dissolving metals are known to reduce both allylic and

vinyllic halogens without migration or geometric isomerization of double bonds. While treatment of di- and tetrachloro derivatives of bicyclo[4.2.1]non-3-ene with sodium in liquid ammonia affords the expected olefin, treatment of the trichloro compound results in the formation of a cyclopropane hydrocarbon, endo-tricyclo[4.2.1.0^{2,4}]nonane. In order to test the generality of the reaction, trichlorobicyclo[5.2.1]dec-3-ene and trichlorocycloheptene have been submitted to Birch reduction. While the bicyclic system yielded exclusively the cyclopropane compound, the monocyclic system gave both norcarane and methylcyclohexene. The latter probably also arises from a cyclopropane intermediate. The mechanism proposed involves the formation of allyl radicals which undergo electrocyclic closures in a disrotatory fashion, when steric restrictions are not too severe, to give cyclopropyl radicals. The last point is illustrated by the reduction of the trichlorobicyclo[3.2.1]octene system, which results in the unique formation of the corresponding olefin.

In this bicyclic series, the synthesis of bicyclo[4.2.1]nonan-3-one has been investigated by other groups. These syntheses have all involved the rather expensive bicyclo[3.2.1]octan-3-one, which after ring enlargement yields a rather impure product. In the present work, optimization of the thermal ring opening of exo-3,3-dichlorotricyclo[4.2.1.0^{2,4}]nonane with elimination of HCl (77% yield) led us to an improved preparation of the desired ketone. Treatment of the monochloro diene thus

obtained, with sodium in liquid ammonia gave bicyclo[4.2.1]-non-3-ene, which on hydroboration and oxidation afforded the ketone in a high purity (>99% by GLC). The overall yield of 20% obtained from 5-hydroxymethylnorbornene compares favorably with the 17-18% yield obtained previously.

RESUME

Il a été montré au cours de ce travail que l'utilisation du dichlorocarbène pour l'agrandissement de cycles présente un grand intérêt synthétique, à condition de pouvoir ouvrir facilement les adduits cyclopropaniques formés. Ainsi, les produits d'addition de dichlorocarbène aux dérivés du norbornène se réarrangent déjà à température ambiante pour donner le système bicyclo[3.2.1]octénique. Par contre, l'addition de dichlorocarbène au bicyclo[3.2.1]octène-2, ainsi qu'à ses dérivés mono- et dichlorés, a conduit à la formation de composés tricycliques beaucoup plus stables, puisqu'ils se sont révélés être absolument inertes à des températures allant jusqu'à 180° ou même 220° dans certains cas.

La stabilité remarquable de ces composés en a fait des substrats de choix pour l'étude de la réduction d'halogénures cyclopropaniques géminés ou en tête de pont au moyen de l'hydrure mixte de lithium et d'aluminium. Ainsi, il a été démontré que ces réactions ne se font pas selon un processus de substitution nucléophile S_N2 , comme admis auparavant, mais plutôt par une attaque directe de l'hydrure métallique sur l'halogène; la formation de carbanions intermédiaires serait de ce fait à l'origine de la retention de configuration observée lors de la réduction de dérivés fluorochlorocyclopropaniques. L'étude systématique de la réduction des produits tricycliques di-, tri- et tétrachlorés a permis d'autre part

d'établir que les halogénures cyclopropaniques sont plus réactifs que les halogénures en tête de pont, eux-mêmes étant plus réactifs que les halogénures d'alcoyles.

L'ouverture de ces dérivés cyclopropaniques en systèmes allyliques par voie thermique peut être accompagnée d'une élimination d'acide chlorhydrique pour donner des dienes conjugués. Ainsi, suivant les conditions choisies, on a obtenu des chlorures de bicyclo[4.2.1]nonényle ou de bicyclo[4.2.1]nonadiényle, Ces ouvertures de cyclopropanes se font avec des rendements variables selon les cas.

L'irradiation directe ou avec sensibilisateur d'état triplet du bicyclo[4.2.1]nonadiène-2,4, ainsi que de ses dérivés mono- et dichlorés a permis d'observer la formation de dérivés cyclobuténiques par fermeture électrocyclique disrotatoire. La présence d'un, puis de deux chlores sur le système conjugué a considérablement influencé le cours des irradiations directes. Ainsi, la distribution des produits cyclobuténiques dichlorés formés à partir du système diénique 2,3-dichloré s'est avérée être très voisine de celle obtenue au cours de la réaction photosensibilisée. Ces résultats ont été discutés en termes d'effet d'atome lourd intramoléculaire dû aux atomes de chlore fixés directement sur le chromophore.

L'utilisation en synthèse des composés chlorés obtenus par thermolyse des adduits cyclopropaniques, nécessite dans la plupart des cas une substitution des chlores par d'autres groupements fonctionnels, ou simplement l'élimination de ces chlores.

La réduction d'halogénures allyliques au moyen d'hydrures métalliques tels que LiAlH_4 , Bu_3SnH ou NaBH_4 se fait aisément. Cependant, ces réactions sont souvent accompagnées d'une migration de la double liaison et mènent par conséquent à des mélanges d'isomères. Le cas des réductions avec l'hydrure de lithium aluminium a été examiné de plus près et a montré que dans tous les cas, l'entrée de l'hydrure et le départ de l'halogène se font de manière synfaciale. D'autre part, aucune trace de produit provenant d'un déplacement nucléophile bimoléculaire simple, $\text{S}_{\text{N}}2$, n'a été détectée. Les résultats obtenus semblent indiquer qu'il s'agit d'une attaque $\text{S}_{\text{N}}2'$ ou $\text{S}_{\text{N}}\text{i}'$ de l'hydrure sur une paire d'ions, sans pour autant que l'on puisse opter définitivement pour l'un ou l'autre mécanisme.

L'utilisation de métaux en solution, comme le sodium ou le lithium dans l'ammoniac liquide, permet non seulement de réduire les halogènes en position allylique, mais également d'éliminer les halogènes vinyliques, sans affecter la double liaison. Alors que les dérivés di- et tétrachlorés du bicyclo[4.2.1]nonène-3 ont donné dans les conditions de Birch l'oléfine attendue, le composé trichloré a donné naissance exclusivement à un hydrocarbure cyclopropanique, l'endo-tricyclo[4.2.1.0^{2,4}]nonane. Afin de déterminer jusqu'à quel point le traitement de systèmes allyliques trichlorés constitue une méthode générale de formation de cyclopropanes, les systèmes bicyclo[5.2.1]décénique et cyclohepténique trichlorés ont été soumis aux mêmes conditions. Alors que le squelette bicyclique

ne donna que le produit cyclopropanique, le composé monocyclique donna le norcarane et le méthylcyclohexène, ce dernier provenant très probablement aussi d'un intermédiaire cyclopropanique. Le mécanisme proposé fait intervenir la formation de radicaux allyles, qui ensuite se ferment disrotatoirement en radicaux cyclopropyles, lorsque les tensions dans les cycles ne sont pas trop fortes. Ce dernier point a été vérifié en effectuant la même réaction sur le système bicyclo[3.2.1]octénique trichloré, qui n'a donné que l'oléfine correspondante.

La bicyclo[4.2.1]nonanone-3 est un dérivé de cette série bicyclique dont la synthèse par différentes voies avait déjà fait l'objet de travaux d'autres auteurs. Ils sont tous partis de la bicyclo[3.2.1]octanone-3 relativement chère et qui mène à une cétone homologue supérieure souvent impure. Dans notre cas, le fait d'avoir amélioré les conditions d'ouverture thermique de l'exo-3,3-dichlorotricyclo[4.2.1.0^{2,4}]nonane avec élimination d'HCl (77% de rendement), a conduit à une nouvelle méthode de préparation de cette cétone. Le traitement du 3-chlorobicyclo[4.2.1]nonadiène-2,4 ainsi obtenu, avec le sodium dans l'ammoniac liquide a donné le bicyclo[4.2.1]nonène-3, qui après hydroboration et oxydation a donné la cétone en question avec un degré de pureté >99%. Le rendement total de 20% obtenu à partir du 5-hydroxyméthylnorbornène est tout à fait compétitif avec les rendements de 17-18% obtenus à partir du norbornène par ces autres auteurs.

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